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Original ARTICLES

EXPERIENCE WITH A NEW ANTICOAGULANT COUMADIN® (WARFARIN) SODIUM

By Daniel H. Goodman, M.D.
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THE DISCOVERY and clinical application of anticoagulants has been one of the most noteworthy contributions in medicine in the past decade. Their usefulness is well established. The increasing use of anticoagulants stimulated chemists to search for an anticoagulant which would be both effective and safe for wide employment by specialist and generalist alike. Such an ideal drug would extend the field of usefulness of anticoagulant therapy generally, and would exert a salutary effect on the grave social and economic implications of thromboembolic disorders.(1)

The criteria for an ideal anticoagulant have been formulated.(1)(2) These include (1) oral as well as parenteral effectiveness; (2) rapid onset of action; (3) satisfactory therapeutic index and freedom from untoward side-effects; (4) no cumulative action or toxicity from prolonged use in ambulatory patients; (5) predictable quantitative relation between dose and anticoagulant effect, and uniformity of response from patient to patient; (6) an anticoagulant activity not requiring daily laboratory control; (7) prompt cessation of effect when administration of the drug is stopped, or when an easily administered nontoxic antagonist is given; (8) low cost; (9) ability of an antagonist to titrate excessive hypoprothrombinemia back to the therapeutic range and (10) a capacity of the anticoagulant to reinduce therapeutic hypoprothrombinemia after administration of a counteractant.

Coumadin® (Warfarin) Sodium, a new anticoagulant, was developed in the laboratories of Professor Karl Paul Link, of the University of Wisconsin, the discoverer of the first oral anticoagulant, Dicumarol. Coumadin Sodium is a potent hypoprothrombinemia inducing agent. It has the following properties: (1) it is soluble in water, it can be administered orally or intravenously; (2) it has great predictability of response; (3) relatively small doses induce a therapeutic hypoprothrombinemia within 24 hours; (4) it yields a smooth extended curve of hypoprothrombinemia; (5) an initial dose of one mg. per kg. of body weight (usually 75 mgm.) orally or intravenously is usually adequate to induce a therapeutic hypoprothrombinemia; (6) a steady controlled level of therapeutic hypoprothrombinemia can be maintained by a single dose of 25 mgm. (one tablet) every second to fourth day, or by a daily dose of about 5 to 10 mgm.; (7) bleeding is readily counteracted by phytonadione (vitamin K_1). A reinduction of therapeutic hypoprothrombinemia is readily effected by Coumadin and (8) no dermal reaction or blood dyscrasias have been observed with Coumadin.

The indications for anticoagulant therapy are becoming well defined. The remarkable efficacy of anticoagulant therapy in preventing postoperative venous thrombosis, pulmonary embolism and thrombophlebitis are well

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known.(3) In clinical medicine, anticoagulants are indicated in the treatment of pulmonary embolism, thrombophlebitis, phlebothrombosis and in carefully selected instances of cerebrovascular thrombosis or embolism, occlusion of the central retinal vein, mesenteric thrombosis, frost bite, and vascular damage from trauma.

A prime indication for anticoagulant therapy is coronary thrombosis with myocardial infarction. It represents an exceedingly important advance in the management of patients with acute coronary occlusion and myocardial infarction. The cooperative study of the Committee on Anticoagulants of the American Heart Association showed that the use of anticoagulants strikingly improves the survival rates of patients who suffered an acute coronary occlusion with myocardial infarction. Thromboembolic complications were reduced by nearly 75 percent and the death rate was decreased by more than one-third.

These findings on 1036 patients led to the recommendation that all patients with coronary thrombosis and myocardial infarction receive anticoagulant therapy in addition to the conventional forms of treatment, unless a definite contraindication exists. Since it is, at best, extremely difficult if not impossible to differentiate between the "good risk" cases and the "poor risk" cases, it is advised that treatment with anticoagulants be routinely employed in cases of myocardial infarction, unless definite contraindication exists.(4) But the wider application of these results awaited the availability of a truly effective and safe anticoagulant. Coumadin most closely approaches the ideal anticoagulant in terms of safety and efficacy.(5)(6) Its use in myocardial infarction should be routine. Coumadin Sodium has no known side-effects. Hemmorrhage from an excessive dosage is not regarded a side-effect. It is an extension of a pharmacologic effect. In those instances where hemorrhagae does occur, it can be readily counteracted by vitamin K_1 or menadione.

The contraindications are similar to those for Dicumarol. Coumadin should not be administered in the following conditions: (1) In all types of purpura and other blood dyscrasias, in which there is a hemorrhagic tendency. (2) Liver disease. Patients with liver disease frequently have hemorrhagic tendencies, which suggests caution in administration of the drug. Nutritional deficiency states and other causes of hepatic insufficiency will require a much smaller amount of Coumadin for induction or maintenance of therapeutic hypoprothrombinemia. (3) Recent surgery on the central nervous system. (4) Ulcerative lesions of the gastrointestinal tract and other inaccessible ulcerations. (5) Dissecting aneurysm, such as a mycotic or berry aneurysm, or a suspected weakening of any vascular wall. (6) Renal insufficiency is only a relative contraindiction. (7) Thromboses in patients with carcinoma of the body and tail of the pancreas. Migratory phlebitis or recurrent phlebitis, which characterizes carcinoma of the body and the tail of the pancreas, is in my estimation a definite contraindication to anticoagulant therapy. In such thrombotic states, there already exists a depletion of prothrombin due to hyperutilization.(8)

The pharmacological action of Coumadin is like that of Dicumarol. It affects blood coagulation by causing hypoprothrombinemia. It exerts its initial effect in vivo after a relatively short latent period. The latency results from the fact that Coumadin has no direct effect on circulating prothrombin, but acts by depressing the hepatic production of this protein. Inasmuch as up to 24 hours are required until all the circulating prothrombin in the body is used, the effect of the drug-induced inhibition of its synthesis is not manifest until some hours have elapsed. Coumadin and similar related anticoagulants inhibit prothrombin production by interfering with vitamin K in the liver synthesis of prothrombin. The effect of Coumadin is opposite to that of vitamin K. Coumadin causes hypoprothrombinemia; vitamin K causes hyperprothrombinemia.

I have used Coumadin routinely in myocardial infarction. I have also used it in the following conditions: thrombophlebitis, phlebothrombosis, phlebitis migrans, cerebral thrombosis, cerebral embolus, pulmonary embolus, congestive heart failure, conversion of atrial filbrillation to regular sinus rhythm with quinidine, status anginosus, chronic rheumatic valvular disease with atrial fibrillation and thrombo-embolic phenomena, axillary vein thrombosis in a patient later proved to have carcinoma of the body of the pancreas.

Patients requiring anticoagulant therapy were given an initial dosage of 50 to 75 mgm. of Coumadin intravenously, after the determina-

tion of prothrombin time. Thereafter, daily prothrombin determinations were made. A single dose of 25 mgm. was required on the average of once every third day. In the hyperreactor, that is, in those individuals who required less of the anticoagulant, 25 mgm. every fourth day was required. The hyporreactor, who required a little more Coumadin, 25 mgm. was given about every 48 hours to maintain a satisfactory prothrombin response. In practically all the cases, a therapeutic hypoprothrombinemia was induced with the average calculated dose given intravenously. Heparin was used during the brief lag period of induction of therapeutic hypoprothrombinemia. It was rarely necessary to use heparin therapy for more than 24 hours, when Coumadin was administered intravenously as the primary anticoagulant.

The intermittent mode of maintenance therapy was admirably suited for ambulatory therapy. With the administration of one 25 mgm. tablet on the average of every third day, equivalent to approximately two tablets or a total of about 50 mgm. per week, there is little to no danger of hemorrhage. It is to be noted that by the intermittent mode of administration for maintenance therapy, each dose is given as the prothrombin time in seconds reverts to normal or conversely as the prothrombin activity in percent begins to rise. Therefore, there cannot be any accumulation of the anticoagulant. Furthermore, this method of administration reduces the cost to the patient, not only in the negligible cost of the drug itself, but in the fact that blood for a prothrombin time determination need be drawn only once a week, and probably even less often than that, when the individual's capacity and response to Coumadin have been observed over a period of time.

The author has had limited experience with the daily administration of Coumadin. However, it has been suggested that a daily dosage of 10 mgm. will suffice for maintenance dosage with adequate safety.(5)(6)

Hemorrhage was encountered in 12 cases, or 8 percent of the cases. With the exception of the patient with the axillary vein thrombosis, who later proved to have a carcinoma of the body of the pancreas with metastases, hemorrhage was characterized by microscopic and gross hematuria. In each case of gross hematuria, hemorrhage was readily and speedily controlled by the intravenous administration of vitamin K_1 (Mephyton) given intravenously. Several cases of hypoprothrombinemia with prothrombin times varying from 45 to 78 seconds were allowed to regress to therapeutic levels spontaneously simply by withholding maintenance medication. These periods varied from 1 to 3 days duration.

In the one case of axillary vein thrombosis in the patient with carcinoma of the body of the pancreas, later proved by autopsy, a rather alarming hemorrhage resulted from the intravenous administration of 37.5 mgm. as the initial dose.(7) This patient began to bleed from each puncture site, and a gross hematuria was noted several hours after the administration of the Coumadin. The anticoagulant had no salutary effect on the thrombotic manifestations. This is readily understood from the study of the pathologic physiology of thromboses due to carcinoma of the body and tail of the pancreas. The enhanced clotting effect in such instances is due to persistent release of trypsin from the tumor bed into the circulation with failure of the antitryptic mechanism.(8) This failure of the continual formation of antitrypsin accounts for the clotting tendency in carcinoma of the body and the tail of the pancreas. In this condition, there is also a marked depletion of the prothrombin due to hyperutilization, rather than due to a primary defect in formation. Therefore, anticoagulants are not only ineffective in preventing thromboses as a complication of carcinoma of the body and the tail of the pancreas, but it definitely increases the hazards of hemorrhage, as was readily demonstrated in this case. As a matter of fact, the hyperreaction, that is, the marked anticoagulant response and bleeding resulting from only a single dose of 37.5 mgm. of Coumadin given intravenously may be a clue to the clinician that the underlying pathological condition causing the thrombosis may be due to a carcinoma of the body and the tail of the pancreas. As is well-known, this condition is extremely difficult to diagnose antemortem, although it may be strongly suspected. Such hyperreaction to Coumadin, when used to treat migratory phlebitis, should lead the clinician to suspect carcinoma of the body or tail of the pancreas as the underlying causative factor.

Anticoagulants have not reached a desired level of usage because of the fear of hemor-

rhage. This fear has been engendered by the shortcomings of Dicumarol and its cogeners. It is the fear of hemorrhage that has given rise to so much discussion of the "good risk" and the "bad risk" patients in evaluation of anticoagulant therapy in coronary artery occulsion and myocardial infarction. In the case of myocardial infarction and other cogent medical indications for anticoagulant therapy, there is only the "good risk" patient in retrospect. With the availability of Coumadin, which most nearly approaches the ideal anticoagulant drug, the danger of bleeding, which will be inherent in any anticoagulant, is certainly minimal and most readily reversible.

Thus, in the opinion of the author, it is no more hazardous to use Coumadin where it is indicated, than to use insulin or digitalis. Certainly, any physician who has ever digitalized a patient or has cared for a diabetic can certainly learn to use Coumadin safely. The undue emphasis on the danger of bleeding has unnecessarily caused many physicians to deprive their patients of the benefits of anticoagulants in thrombo-embolic conditions. This need no longer be the case. The use of anticoagulants need not be reserved for those in the specialties, but can readily be a most potent tool in the hands of the generalist, who takes the time and the effort to learn the few details for most effective administration. All that is needed are proper laboratory facilities and trained personnel for performing the prothrombin clotting time by the single stage method (Quick or Link-Shapiro modification).

Summary: Coumadin has been used in 150 clinical cases requiring anticoagulant therapy. It can be given intravenously as well as orally. A single intravenous or oral dosage of 50 to 75 mgm. will give a therapeutic hyoprothrombinemic response within 24 hours. It has a great predictability of response. A therapeutic hypoprothrombinemia can readily be maintained by a daily dosage of 10 mgm. or an intermittent dose of 25 mgm. at 3 day intervals. Bleeding, which has occurred in 8 percent of the author's cases, manifested primarily by hematuria, was readily controlled by intravenous vitamin K_1 (Mephyton). No side reactions or toxic reactions, such as dermal reactions or blood dyscrasias, have been observed with Coumadin. It is the opinion of the author that Coumadin can be used in the routine treatment of acute coronary artery occlusion with myocardial infarction, and other conditions requiring anticoagulants, with a degree of safety on the part of the clinician, that is not available in other anticoagulants. Coumadin offers the advantage of low cost to the patient, a factor of particular importance in long range ambulatory treatment. Less frequent prothrombin determinations are needed because of the smoothness of the prothrombin response and absence of cumulative effect.

The author agrees with others(5)(6) that Coumadin possesses properties which make it most nearly the ideal anticoagulant of all those available to date. It deserves universal usage as an anticoagulant.

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PATHOPHYSIOLOGY AND VASOCONSTRICTIVE THERAPY FOR MENORRHAGIA AND HEMORRHAGE ACCOMPANYING PARTURITION

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MENORRHAGIA, according to Bell(1) is excessive or prolonged menstrual bleeding. Metrorrhagia refers to uterine bleeding which is not connected with the menstrual cycle. Lesions, such as cancer, other types of tumors, and abortions can produce uterine hemorrhage. These menorrhagie disturbances, Bell recorded, are not understood clearly. Such disorders might be due to ovarian tumors and various systemic disorders. These physiologic or functional disturbances may show hypertrophic cystic endometria or membranous dysmenorrhea, but the endometrium is often normal and may be in the early or late proliferative phases. Bell records that 75% of the curettements from such cases show normal mucosas. Cancer produces uterine bleeding more often during menopause than in younger females.

Our current interest in menorrhagia stems from our recent post-partum lochial studies. Such patients were treated with a vasoconstricting agent (Kutapressin).* 2 cc. of this material was injected intragluteally daily after delivery. It was surprising to learn that many of these nursing mothers reported significant increases in their lactogenic responses during the above therapy. Perhaps the suppression of such lochial discharges helped to conserve the highly important electrolytic and high protein-containing elements from the uterine discharges for the benefit of these nursing mothers' well being.

An attempt will be made to demonstrate, in this study, the relationship between such supposedly unrelated topics as menorrhagia, chronic passive uterine congestion with venous and arteriolar vasodilatation and excessive uterine bleeding during parturition, which appear to have similar points. Such correlated manifestations appear to be controlled adequately by appropriate vasconstrictive measures. Furthermore, certain observations exhibited by the human female are under the influence of basic physiologic and pathologic processes which can be observed rather readily also in certain exudative types of lesions in both sexes.

We have attempted to focus the clinicians' attention on some of these commonly occurring sero-sanguinous discharges from wounds which can become markedly debilitating(3) to such patients if allowed to persist and drain freely without adequate therapeutic control.

Since the effective control and the desirable suppression of such fluid loss to the body's economy appears sound, it may be important to pursue further these investigations for the adequate control of the edematous states observed in other diseases with similar vasoconstrictive procedures.

It was observed that cases of ivy poisoning responded adequately to the use of Kutapressin(4). This material was administered parenterally (subcutaneously or intramuscularly). It was non-toxic and did not produce those distressing allergic side effects which have been observed on occasion with the use of various liver extracts when administered parenterally. Vasoconstriction was produced in the terminal arterioles and capillaries within a matter of about 10 minutes or less after its administration(5).

The concommitant edematous state which accompanies inflammation produces passive congestion in the affected tissues and organs. This undesirable edematous state is characterized by both arteriolar and venous congestion. The vascular structures which supply such an edematous area are dilated markedly. It has been reported that the venous pressure is elevated markedly in patients who exhibit edematous tissues. Indirect (Gaertner) and direct (Cohen) determinations of venous pressures, following the injection of Kutapressin, showed a reduction of venous pressure(6).

The importance of edematous states with their proper control becomes obvious, parti-

*Kutapressin, supplied by Kremers-Urban Company, Milwaukee 1, Wisconsin.

ularly when one realizes that edema is one of the main findings which accompanied such inflammatory processes with many diseases.

Edema is present also in the post-gravid uteri. The profuse exudative (lochial) response which follows childbirth can be debilitating for any woman especially if the volume of flow has become pronounced. Hence, its early suppression and control appears to be accompanied by a more rapid uterine involution with a highly desired conservation of those important electrolytic and protein fluids which otherwise would become lost to the patient.

It is not a great jump from the proper vasoconstrictive control of post-partum lochias to the use of vasoconstrictive therapy for patients with menorrhagia. We believe our readers will discover possibly several clinical correlations between these two phenomena.

The blood supply of any tissue or organ is composed of the arteries with their terminal counterparts, which connect with the venous portion of the circulation by means of venules which carry the blood to the larger veins, and thence to the heart. This system is but a small part of the complete picture. Insufficient stress has been placed heretofore on the terminal circulation and therefore, many clinical investigators have not found it expedient to study this highly important phase of the circulation, and particularly the micro-circulation.

We have found it valuable to consider this aspect of the circulation while studying the vasopressor effects observed with the use of Kutapressin on the terminal vascular components. In order to understand, for example, those changes which accompany menstruation, it is necessary to describe the minute changes which take place in the peripheral vascular areas of both the arterial and the venous uterine components.

Uterine Blood Supply

Blood vessels are found in the lateral uterine ligaments(7). These vessels go to the subepithelial connective tissue in the serosal portion of the muscular area in the uterine wall where they spread in all directions. The muscles and serosal portion of the uterus are supplied by an extensive vascular plexus. At the surface of the subepithelial layer, both capillary and venous plexuses are found.

The uterine lymphatics are supplied by anastomosing channels found in the muscular and also the mucous layers, and these lymphatics form a plexus in the serosal layer. They exit via the lateral ligaments and also from the connective tissue of the pelvis and run to the lower lymphatic nodes which are located in the lumbar areas.

Uterine Nerve Supply

Both the spinal and the sympathetic nerves supply the uterus. These structures come from the ganglionic pelvic plexus and enter the serosal layer of the uterus and then supply the muscular areas where they form diffuse plexuses. From these plexuses the sympathetic motor nerves enter the walls of the blood vessels and their muscle layers.

Uterine Histology and Gross Anatomy

The body of the uterus contains tubular, slightly branched glands which traverse the breadth of the mucosal layer in a manner which is similar to a cork screw. Their function is for epithelial regeneration rather than for glandular secretion.

The cervical portion of the uterus contains markedly branched glands which secret a sticky mucous material. The mucosal layer covers the uterine cavity, whose surface is usually in close apposition but might be separated by debris which is composed of dead cells from epithelial sloughs(7).

The uterus is pear-shaped and is separated into the fundic and cervical portions. The fundic area has 3 layers. From outside inward, first there is the serosal (peritoneal) layer, then the myometrial layer which has two chief sections. The superficial (inside) third layer is called the functional stratum which produces many of the changes seen during menstruation. The deeper and thicker layer, the lower stratum, is not concerned with menstrual changes. The top layer (functional) may be lost completely during each menstrual period(8).

The Human Menstrual Cycle

From the first to the fourth day, the uterus has begun its menstrual cycle in a normal human female. The estrogenic phase of the menstrual cycle takes place from the fourth day until a day or two following ovulation. The endometrium, during this time, grows from two to three times in thickness because it is under the influence of estrogens. The ovarian follicle

begins to mature and proliferates to the surface. The corpus luteum, which appears following ovulation, is readied for secretion a day or two after each ovulation, and the estrogenic phase begins a day or two following ovulation. From the 4th to the 16th day, the endometrium is in the estrogenic phase. After this time, the interval phase occurs when the endometrium is repaired but the effects of progesterone do not become evident. Because of the progesterone secretion, this phase is termed the progestational phase. If conception occurs at this interval, it is called the progravid phase. If pregnancy does not take place, the secretory phase comes into being and the epithelial cells begin to secrete. This portion of the cycle occurs about 2 days following ovulation and lasts usually 12 to 14 days. The ischemic phase occurs during the last 2 days of the secretory phase. It is produced by the impairment of the blood supply to the superficial part of the endometrial functional layer. Hence, this layer tends to become ischemic(9). A hormone deficiency due to the vasoconstriction in the coiled arteries then takes place. These arterioles become jack-knifed before menstruation occurs. Hence, endometrial retraction with uterine bleeding may occur due to the withdrawal of estrogen. The breakdown of the endometrial layer is caused by failure in the supply of progesterone. The basal cell layer remains intact during menstruation since it has its separate blood supply.

Maximow and Bloom(10) recorded that four intervals of activity can be ascertained in the endometrial cycle: (1) The follicular phase comprises the first half of the cycle and is associated with a rapidly growing graafian follicle. (2) Progravid (lutein phase) is associated with a functioning corpus luteum. (3) Ischemic phase is caused by very little blood passing through the coiled arteries. (4) The menstrual phase is associated with endometrial injury which produces extravasation.

It may be well to recall that the progravid phase features a thickening of the endometrium which produces an increase in its secretion with the presence of both **edematous fluid** and intracellular secretion. About 13 to 14 days after menstruation, the ischemic phase occurs in the non-gravid uterus. The coiled arteries begin to constrict about a day or so prior to menstruation. This constricting action blanches the superficial layer for hours at a time. Hence, involution and shrinking of this superficial layer occur with the loss of its secretion which is composed of edematous fluid and water.

Physiology of Menstruation

With the onset of menstruation, the coiled, constricted arteries open for a short time. Blood exudes from these ruptured vessels into the stroma of the uterus and thence to the uterine cavity. The severed ends of the uterine glands and blood vessels pour out blood which soaks the uterine debris. Uterine bleeding comes from both arterial and venous origin. Usually about 35 cc. of blood is lost during a regular menstrual episode.

Fulton (11) claims that, from 4 to 24 hours prior to the menstrual outflow, there is constriction in the uterine coiled arteries for several hours. Hematomas may be formed by the dilating arterioles and capillaries which bleed for only 30 seconds to a few minutes. Then other coiled blood vessels dilate, hemorrhage, then constrict, but not simultaneously, since various areas go through the same cycle at different intervals.

The Terminal Blood Vessels

Sodeman (12) recorded that blood flow through the capillaries varies with both location and need. For example, with exercise, increased blood flow and oxygen supply, 20 to 50 times as many capillaries open as when the tissues are resting. Those capillaries which communicate directly from arteriole to venule remain open, but other branching channels (A-V shunts) are not always open.

These points can be observed clinically rather easily. If a recently exercised patient is placed in a supine position and a direct venous pressure reading is attempted, the venous blood will spill over the Lester Cohen measuring tube.* However, if the same patient rests 15 minutes prior to attempting this same procedure, the venous blood will not rise high enough to spill over because the venous pressure tends to decrease with rest after exercise.

The walls of the capillaries are composed of thin endothelial cells. These capillary walls act similar to semi-permeable membranes which allow white and red blood cells, even experimentally injected particles, to transverse these walls at the juncture points between these cells.

*The Lester Cohen venous pressure recording apparatus is manufactured by the Becton-Dickinson Co. and is a handy method for determining direct venous pressure readings.

Here the intercellular cement is found, and this substance may be involved markedly with the process known as capillary permeability. The intercellular cement is said to be composed of a mesh of calcium proteinate. This mesh is thought to exhibit tiny holes of different sizes which allow various liquids and solutions to pass rather easily(13). In this region certain dispersing fluids, as hyaluronidase, dissolve the intercellular cement and thereby allow an increased flow through such an area. Capillary pressure, according to Sodeman, at rest and at heart level, is above the osmotic pressure of the plasma proteins on the arterial side. This capillary pressure is below the osmotic pressure on the venous side. It can become lowered by arteriolar constriction, while dilatation produces an increase in capillary pressure.

According to Sodeman(14), arterioles and venules are connected by arteriovenous capillaries which are incompletely surrounded by smooth muscle cells. Exuding from these thoroughfare channels are true capillaries through which the fluid is controlled by sphincters at their origin from the arteriovenous capillaries. The true capillaries rejoin the arteriovenous capillaries distally. Phasic dilatation and constriction of the arterioles, arteriovenous capillaries and precapillary sphincters (vasomotion), produce periods of filtration followed by periods of fluid reabsorption.

Sodeman observed the effective hydrostatic pressure was the differential pressure between the tissue and capillary pressures, while the effective osmotic pressure was the differential osmotic pressure between the plasma and the extravascular fluid(15).

Venous Pressure

Sodeman(16) contributed a very important point when he stated that even an increase of 9 millimeters of water in the venous pressure can produce a tendency for the formation of an edematous state because of the predominance of filtration over reabsorption. Venous pressure appears to be a very labile phenomenon. This venous pressure is a measure for the tension of blood in veins. According to Pullen(17), it is the residual pressure from the level of the heart's right auricle to the place where this pressure is being measured. Placing the area to be measured at heart level negates the action of gravity when the patient lies down. The normal venous pressure reading is between 4 to 10 cm. of water or 3 to 8 mm Hg.(18). Any sort of obstruction in this system tends to raise the pressure. When it reaches 16 cm. of water pressure, the presence of edema usually can be ascertained clinically. Hence, the verification of an edematous state can be rather an easy scientific procedure with the use of a direct type of venous pressure measuring apparatus.

Functional or Physiologic Menorrhagia

At the outset of this paper we recorded Bell's findings in relation to the production of this type of uterine bleeding. This form of uterine hemorrhage might be produced by physiologic rather than by anatomic disturbances. Such physiologic disruptions are not understood readily, for no definite explanations have described the exact reason or reasons for such derangements in uterine physiology which produce this particular type of menorrhagia.

We observed this disorder quite commonly in our separate practices. Treatment has ranged from tamponade to the use of many types of glandular therapies, all without too much success.

In those cases with functional uterine hemorrhage, the uterus exhibits marked vascular congestion with profuse edema, according to Boyd(19). Furthermore, the importance for controlling hemorrhage in the terminal portion of the vascular tree has been emphasized by Mac Bryde(20) who focused attention on the importance of controlling the capillary areas for proper hemostasis. He stated that the capillary bed assumes "ominous significance" in cases of trauma which produce hemorrhage. He recorded that each cubic millimeter of blood is exposed to approximately 4 square feet of endothelial surface (mostly in the capillaries) in its traverse of the circulation(21). As we noted previously, the arterioles and capillaries of the uterine areas are involved obviously in cases which exhibit physiologic menorrhagia. Hence, the proper therapeutic attack should incorporate the adequate control of these peripheral vascular areas by means of vasoconstriction.

Therapy

The pharmacologic approach to the treatment of menorrhagia must depend mainly upon those drugs which possess the power of vasoconstriction. Perhaps the most powerful drug of this type is epinephrine which appears to be the

main factor for producing a rise of systemic blood pressure because of its property of vasoconstriction(22). The ergotoxine and the ergotamine group of drugs appear to be related closely chemically and pharmacologically(23). These preparations have been employed to check hemorrhages of the uterus, but Sollmann claims these drugs are probably of little value apart from obstetric conditions(24). Apparently these drugs do not increase systemic blood pressure unless ergot is injected intravenously(25). Histamine lowers systemic blood pressure by dilating the capillaries. Posterior pituitary gland preparations can produce persistent vasoconstriction(26), but to our knowledge, these preparations are not employed usually to control uterine hemorrhages adequately.

Recently, while studying the effects of Kutapressin on the capillary bed in the temporal bulbar conjunctiva with a capillary biomicroscope, Lee(27) observed arteriolar constriction in 10 patients; he reduced velocity of blood flow in 9 patients, and augmented responsiveness to epinephrine in 13 patients, and noted an increased spontaneous vasomotor action in 6 of the 14 patients who were studied. Kutapressin was dropped on the conjunctival capillary bed of 14 human patients in this research. For this work, the Kutapressin was labeled RB11-40.*

The above study readily demonstrates that Kutapressin vasoconstricts the capillaries and arterioles in man. Similar observations, which demonstrate the clinical effectiveness of Kutapressin for the treatment of various diseases, have appeared in the medical literature sporadically. Clinical improvement was noted in various types of exudative diseases, but each of these diseases had one outstanding and important point in common. Each disorder exhibited the presence of tissue edema, which is one of the cardinal signs for inflammation(28). Kutapressin did not produce a rise of systemic blood pressure in any patients, although it produced capillary and arteriolar vasoconstriction in these cases.

Increased venous pressure can be an important finding which accompanies tissue edema. Of the two extremes in venous pressure, the low phase of venous pressure can produce shock and thrombosis, while a high venous pressure tends to increase edematous states. There is no apparent relationship between the range of venous and arterial pressures, according to Christian(29).

In the arterial component of the vascular tree, arteriolar constriction produces somewhat of a fall in pressure in the capillaries, while an increase in venous pressure produces an increase in capillary pressure(30).

Starling's hypothesis of fluid balance is in accord with the direct pressure readings found in human capillaries. A fall in blood pressure does not stop in the area where the arterioles develop into the capillaries, but it continues unabated throughout the capillary loop. The average blood pressure in the arteriolar areas is above, and in the venous limb, it is below the osmotic pressure of the plasma proteins, according to White(31).

Kutapressin Therapy

An increase of nine millimeters of mercury in the venous pressure, according to Sodeman(31) can give rise to an "edema tendency" due to the predominance of filtration over reabsorption. Conversely then, a decrease of the same amount in the venous pressure should help to alleviate such an edematous state, if present.

We have noted a decrease from 30 to 60% in the direct (Cohen tube technic) and also the indirect (Gaertner) venous pressure readings in patients after the clinical use of Kutapressin. Since edema is present in many cases with functional or physiologic menorrhagia, we treated 36 such patients with 2 cubic centimeter doses of Kutapressin which were administered subcutaneously daily to each patient.

In every case, we observed a marked reduction in the previously heavy menstrual flows in these patients who related that the reduction in the amount of uterine hemorrhage could be noticed within twelve hours after the initial administration of Kutapressin.

These findings are quite similar to the data we recorded previously in cases with postpartum lochial discharges which were treated with Kutapressin(33). There were no complications from this type of therapy which was well received by these debiliated patients.

Rather recently our group of investigators observed another application for the use of vaso-

*RB11-40 was regular Kutapressin prepared without the addition of ½% phenol. It was found that Kutapressin with ½% phenol caused vasodilatation due to local irritation when it was dropped directly on the conjunctivae of human subjects. Hence, Kutapressin without phenol was used for this particular study by Lee.

constrictive measures in the treatment for exudative phenomena. This therapeusis concerned patients who underwent cholecystectomies and had drainage tubes inserted to facilitate more rapid convalescence. Such post-operative serosanguinous biliary discharges in the surgical dressings were noted to dry up much faster when Kutapressin was administered to these cases with daily doses of 2 cubic centimeters (administered subcutaneously).

We noted that such abdominal discharges became scanty around the 3rd post-operative day when the abdominal drains were removed. By the 5th day, the wounds were practically dry.

These observations resemble those findings which were noted with the post-partum lochial discharges which cleared around the same length of time after delivery. In both types of cases the healing rates appeared to be far more rapid than with those many cases who did not receive the vasoconstricting benefit from Kutapressin.

However, for those colleagues who desire to effect a faster and more complete eradication of such post-operative abdominal discharges following biliary surgery, we suggest that daily 2 cubic centimeters subcutaneous injections of Kutapressin be employed to assure more complete and faster wound healing plus the rapid elimination of drainage in those patients who submit to extirpations of the gall bladder. This vasoconstrictive procedure can be administered with safety. No contraindications for its use are known at this time, and no ill effects have been encountered during the time Kutapressin has been used clinically by our group.

According to Overman(34) vasodilatation, per se, of the capillary bed leads to an increased filtration pressure in the capillaries. Also, there is an increased accumulation of extravascular fluid which is largely deproteinized plasma. The volumetric pressure relationship across the endothelium becomes disturbed, which leads to further fluid extravasation. Under normal conditions the process of filtration exceeds reabsorption into the capillaries. The excess fluid is absorbed by the lymphatic drainage. These fluid accumulations, according to Overman, which result from an excess of filtration over reabsorption and lvmph drainage can and do increase local lymphatic obstruction and thereby produce an added amount of edema formation. Overman observes "There is, of course, ample physiological rationale for the employment of vasoconstrictive measures in combating edema."

Our therapeutic procedure, in this study, was employed to prevent excessive menstrual flooding in functional cases of menorrhagia. However, the same procedure for combating hemorrhage, and even the formation of edema where such exists, has not, to this date, confronted us with any apparent contraindications for the use of these vasoconstrictive measures.

A patient who was 8 months pregnant developed a severe acute enteritis with a moderate amount of rectal bleeding. She was given 2 cc. of Kutapressin subcutaneously to control this bleeding due to gastrointestinal hemorrhage. The medication proved very effective by stopping the bleeding. Later that evening she went into active labor and delivered a premature male infant, whose weight was 5 pounds, 4 ounces. This infant died a few days later because of paratyphoid fever. It was our opinion that the enteritis produced early labor. Later findings proved that paratyphoid fever was the cause. Apparently she had infected her child with this disease.

The amazing finding at the time of this delivery, which was about 6 hours after Kutapressin administration, was that her labor was exceedingly easy. She lost approximately 10 cc. of blood during the entire course of her labor which was aided with the application of perineal forceps (Simpson). This very light blood loss at the time of delivery is what we would expect in the light of our previous experiences with this vasoconstricting preparation. On many occasions, during Cesarean sections, we have witnessed a marked hemostasis during such major surgical procedures with Kutapressin. The same hemostatic results when Kutapressin is administered pre-operatively in cases undergoing tonsillectomies(35) further fortifies our contention that this material acts as an extremely valuable vasoconstrictor of the capillaries and arterioles. In light of our current findings by employing Kutapressin in women who are undergoing the onset of labor, we are now administering this material routinely to conserve the hemapoietic elements which otherwise might be lost by active uterine hemor-

A B C

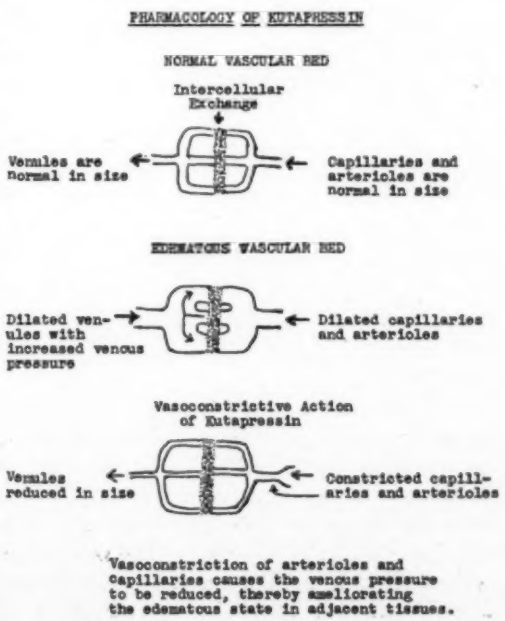
Cyclical changes in the endometrium. A. Post-menstrual (oestrin) phase. B. Intermediate stage (fifteenth day). C. Premenstrual (progestin) phase (23rd day). All specimens are curettings. x 67.

rhages. We also have cause to believe that this vasoconstricting procedure may prove to be very valuable in controlling certain cases of threatened abortions. Such cases have been treated in a highly adequate manner to prevent possible uterine hemorrhage with abortion. To date, we have experienced no failures, although our case series is small, and the placental separations may not have been complete.

Hence, we urge that Kutapressin be administered at the onset of active labor, certainly before or at the latest during the second stage of labor. Daily Kutapressin injections should be continued to control the post-partum lochial discharges, to control possible hemorrhage, to foster a more rapid uterine involution, and to give such patients the benefit of an increased lactogenic response, particularly if the mother desires to nurse her offspring.

We observed that, after the delivery of the placenta, the Kutapressin treated mothers' uteri became firm even without the use of oxytocic agents, although we continue to give one injection of this latter material immediately after the delivery of the placenta just to be on the safe side.

It has been our experience also that there is no difficulty of the separating placenta becoming trapped by the uterine walls. We found that deliveries of the placentas where not impeded in any manner when Kutapressin was


PHARMACOLOGY OF KUTAPRESSIN
NORMAL VASCULAR BED
Intercellular Exchange
Venules are normal in size
Capillaries and arterioles are normal in size
EDEMATOUS VASCULAR BED
Dilated venules with increased venous pressure
Dilated capillaries and arterioles
Vasoconstrictive Action of Kutapressin
Venules reduced in size
Constricted capillaries and arterioles
Vasoconstriction of arterioles and capillaries causes the venous pressure to be reduced, thereby ameliorating the edematous state in adjacent tissues.

administered before or during labor.

Recently we delivered an adipose, chubby woman with a very shallow pelvis. She had an occiput posterior presenting child. The patient experienced great difficulty attempting to bring down the child's head. A pudendal block anaesthesia finally relaxed her perineal musculature so that, at length, the fetal head descended enough to allow Simpson forceps to be applied to the head. It was rotated and the child was delivered. The baby was cyanotic, and the child's upper respiratory tract was full of mucus. Oxygen therapy and suction helped to restore proper breathing and good color to the infant.

About four hours following this delivery, the child experienced several severe attacks of hematemesis. A careful examination of the child revealed no apparent cerebral pathology nor intestinal obstruction. One cubic centimeter of Kutapressin was administered intragluteally to the child to control the apparent gastric hemorrhage. In the matter of four hours following the above procedure, the child stopped vomiting blood, and the infant made an uneventful recovery with a dose of one cubic centimeter of Kutapressin administered intragluteally daily for 3 days. When hematemesis occurs, as it does at times following difficult labors, it might be caused by the swallowing of toxic and very irritating material during its descent through the birth canal. Washing out the infant's stomach with physiologic saline solution, which is recommended at times, will not control gastric hemorrhage if present. Furthermore, we do not have much faith in the efficacy of vitamin K as a coagulant for the adequate control of those cases with internal hemorrhage.

Hence, we suggest the use of Kutapressin in such cases, since its administration is both very safe and easy to use. Furthermore, and by far more important, it may prove to be a life-saving procedure for such cases with internal hemorrhage.

Some of our colleagues have asked just how quickly the effects of Kutapressin (evidenced by arteriolar and capillary vasoconstriction) can be expected. We maintained repeatedly that these effects appear to be almost instantaneous. We observed vasoconstriction of the skin in seconds after this medication had been administered. Changes noted by the dropping of venous pressures after the use of Kutapressin have been similar, as has evidence for the control of capillary hemorrhage very soon following the administration of this drug, also for treating severe cases of angioneurotic edema and nose bleed. The above contention appears to be confirmed, because Friedberg(36) found the normal circulation time (arm to tongue test) to be from 9 to 16 seconds.

Sodeman(37) feels that many other factors might be responsible for the decreases in venous pressure which we have observed following the use of Kutapressin. "These relate to the degree of this drop and its statistical significance, to the clear cut action of the Kutapressin, to the generalized versus localized action of the drug and other factors. . . . For example, that the material if acting locally in certain areas of the body could shift blood mass and create differences on that basis."

However, we have good cause to believe that this vasoconstricting property of Kutapressin is generalized in nature. We have observed its action in many portions of the body and in various and sundry types of disease processes, some of which have been mentioned heretofore in this paper.

The reaction to inflammation also affects practically every part of the human organism. The presence of edema, an important finding, which is associated with inflammation, might tend to become more or less localized. Yet the therapeutic action from the use of Kutapressin appears not to be localized to any particular area. On the contrary, the effects from Kutapressin therapy appear to be quite generalized in nature. Hence, we cannot agree with those suggestions which Professor Sodeman kindly offered in our behalf.

Dr. Richard E. Lee(38) believes that vasoconstriction which is produced through the action of Kutapressin produces a drop in venous pressure not alone from the vasoconstriction on the arteriolar side only. He thinks the reduction in the amount of blood which flows through the capillary vessels, per se, might be produced by the vasoconstriction. However, a compensatory dilatation of the arteriovenous shunts might take place to keep such veins filled. Peripheral venous dilatation of the larger venules and small veins in certain key areas, such as the splanchnic, might aid in producing

this drop of venous pressure. Lee thinks this latter action would act to trap the blood in the distal radicals of the venous tree, which would constitute a far more effective method to reduce (venous) pressure in the great veins of the body.

We support the suggestion advocated by Dr. Lee, because the above theory appears quite logical and is well within our concepts which have been culled from our varied clinical experiences with this vasoconstricting agent, Kutapressin. Incidentally, our clinical findings appear to be also in accord with those experimental observations made by Dr. Lee for his highly interesting biomicroscopic studies which we have abstracted heretofore.

Hartroft(39) wrote recently: "The catastrophe of fatal gastro-intestinal hemorrhage strikes, and often fells at a single blow, individuals still in the prime of life, and the critical diagnosis, treatment and management of these cases is therefore doubly important. I hope that in the future we physicians will be faced with an ever diminishing number of this type of autopsy. We eagerly await newer discoveries and advances which will stay this tragic series of events culminating in fatal hemorrhage of gastro-intestinal origin."

Sudden death can occur because of any type of serious, uncontrolled bleeding. We hope the information we have presented in these pages will prove to be a major step for eliminating all types of internal capillary hemorrhage which has plagued clinicians throughout the ages.

Summary

Basic pathophysiologic relationships are described which relate to menorrhagia, chronic congestion, various aspects of the arteriovenous system and uterine hemorrhage during parturition. The process of edema formation is considered with the exudative findings in various diseases such as poison ivy cases and the lochial discharges which follow obstetrical deliveries and the abdominal discharges which follow cholecystectomies. The value of direct and indirect venous pressure recordings is discussed also. A short review of the anatomic and physiologic findings of the human uterus is discussed with emphasis being placed on the terminal vascular supply of this organ. The physiology of menstruation is then reviewed with emphasis being placed on the terminal vascular supply.

The entity known as functional or physiologic menorrhagia is reviewed along with a new therapeutic attack through the vasoconstriction of the arterioles and capillaries. Emphasis is placed on the role played by the venules of the arteriovenous areas. The rationale of Kutapressin therapy is explained though its vasoconstricting effects on these vascular areas. Emphasis is placed on the lowering of the venous pressure readings which serve as a measure for the extent of these edematous states which accompany the basic and highly important presence of inflammation.

Several current comments and opinions from expert investigators are discussed briefly in our attempt to give an understandable and an applicable account of the modus operandi which is connected with Kutapressin therapy. Several clinical experiences are related in order to correlate both the biologic and clinical aspects of various diseases with this vasoconstrictive therapeutic approach. Emphasis, in this respect, is placed upon controlling hemorrhage during the second and third obstetrical stages with this vasoconstrictive treatment. Our recent findings indicate the therapeutic action from Kutapressin is not of a localized nature; its action is exceedingly rapid as is its efficacy and spontaneity.

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RECURRENT PULMONARY DISEASE IN CHILDREN THE SINO-BRONCHIAL SYNDROME

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AN AVERAGE child might contract by chance one or two significant respiratory infections a year, but should bronchitis, or pneumonia, or croup reoccur every few weeks, then some factor other than random exposure to infections must be considered. Recurrent pulmonary infections may present such a serious problem that the family abandons home and job in the desperate hope that a change of climate will prove beneficial. Unfortunately, the migration often fails in its purpose.

In childhood, a common source of repeated pulmonary infections is purulent drainage from the paranasal sinuses – the so-called sino-bronchial syndrome. This condition has been known by many other names, i.e. chronic sinusitis associated with cough, nasopharyngeal and mediastinal lymphadenopathy, chronic non-specific cough in children, etc. It is defined as a subacute or chronic infectious process involving the mucosa of the paranasal sinuses, with secondary implantation of infection upon the mucous membrane of the bronchi through postnasal drainage and with subsequent production of hilar infiltration and focal pulmonary lymphadenopathy(1).

This paper describes the mechanisms responsible for sinusitis and its pulmonary complications, with special reference to management utilizing positive-pressure inhalation of aerosol medication.

MECHANISM

The knowledge that the paranasal sinuses are incompletely developed in early life has resulted in the common misconception among physicians that sinusitis does not occur in children, yet, it ranks as one of the most common diseases of childhood(2).

Of the several sinuses, the maxillary is the most commonly involved in children. Its cavity is well developed at birth and maxillary contents have been reported in stillborns. The ethmoidal cavities are present at birth but remain small under five years. The sphenoid sinus is very small during the first year, and the frontal sinus is rarely visible roentgenologically before the third year(3).

The sinus cavities connect with the nasal passageway by relatively small openings which easily become obstructed. Children are particularly vulnerable to nasal obstruction because of their frequent upper respiratory infections, their inadequate removal of nasal mucus by "blowing" and their abundant lymphoid tissue which readily hypertrophies with infections. When drainage from the sinuses is impaired, the retained secretions become thickened and may become invaded by virulent organisms. This material discharges into the nasal cavity and passes into the nasopharynx more readily than through the external nares, thus a considerable postnasal drip may be present without evidence of a "running nose." In the upright position, the material passes into the pharynx and is usually swallowed. However, when a patient is asleep, this drainage may be aspirated into the lower respiratory tract since swallowing is more difficult without the aid of gravity and because the awareness of accumulated secretions in the pharynx is decreased with sleep. Experimentally, it has been shown that lipiodol instilled into the paranasal sinuses will drip into the lungs particularly when asleep(4). The aspiration of nasopharyngeal material initiates the cough reflex. If the aspirated material contains virulent organisms, infection of the bronchial mucosa and the associated lymph glands follows. Chronic implantation of such infectious material in the bronchial tree is assumed to be a common cause of bronchiectasis(4).

CLINICAL FEATURES

SYMPTOMS:

(a) **Cough** – A cough which is more pronounced at night (when recumbent) or on awakening (more aware of accumulated secretion) is characteristic of the sino-bronchial syndrome. In contrast, the cough of other types of infectious bronchitis is more pronounced on exertion and usually diminishes when at rest. (b) **Laryngeal Irritation** – Recurrent attacks of croup or nocturnal hoarseness occur by virtue of irritation of the larynx by the postnasal drainage. (c) **Gastric Irritation** – Epigastric and periumbilical pain may occur, (sometimes accompanied by nausea or vomiting) primarily at long

intervals following meals, as before breakfast or in the late afternoon before supper. These symptoms are due to gastric irritation and perigastric lymphadenitis resulting from the swallowed purulent drainage. (d) **Fetid Breath** – In the absence of extensive caries, a chronic "bad breath" in children is usually due to the odor of infected material emerging from the sinuses. (e) **Nasal Symptoms** – Excessive, thickened nasal secretion, particularly when there is considerable accumulation of mucus in the nose each morning, is indicative of infection in the paranasal sinuses. Discoloration and thickening of the mucus indicates bacterial contamination of the sinus contents. Edema and hypertrophy of the nasal mucosa may result in blockage of the nasal passageways necessitating mouth breathing. However, postnasal drainage from the sinuses may occur without obvious impairment of breathing through the nose. Nosebleeds may occur as the result of local irritation.

PHYSICAL FINDINGS:

(a) **Nasal Passageways** – Purulent material may be present in the nasal passageways or seen emerging from beneath the turbinates. The nasal mucosa may be pale in appearance if allergy is the primary factor responsible for mucosal edema but reddened if infection is present regardless of the presence or absence of allergy. (b) **Pharynx** – A purulent discharge frequently can be seen running downward from the nasopharynx particularly if the patient gags. On occasions no drainage can be seen at the moment, but the posterior lymphoid tissue is hypertrophied giving the appearance of "the granular pharynx." The tonsils and particularly the adenoids may also be irritated and exhibit enlargement and inflammation. (c) **Lymph Glands** – Enlargement of the cervical lymph glands may occur as the result of extension of infection from the pharynx or tonsils. (d) **Chest** – Pneumonia, bronchitis or bronchiectasis occurring as the result of aspiration of sinus drainage gives the usual findings on auscultation. However, the sino-bronchial syndrome may result in considerable cough without the presence of abnormal chest findings on physical examination. The roentgenogram indicates hilar adenopathy and prominence of the major bronchovascular markings particularly in the dependent portions of the lung. (e) **Sinuses** – Tenderness or redness over the involved sinuses is rarely present in children. However, roentgenograms usually indicate sinusitis, except in the early stages.

TREATMENT

Treatment of the sino-bronchial syndrome must be directed toward the sinusitis as well as the pulmonary complications. Too often the troublesome night cough, the cervical lymphadenitis, the laryngitis or the bronchopneumonia receive exclusive attention. Antibiotics given for these complications of sinus discharge usually result in temporary improvement of the sinusitis but unless adequate drainage of the sinus is established, the retained secretions may again become purulent and the complications of sinus drainage will reoccur.

INTRANASAL MEDICATION:

Recent years have seen great improvement in preparations for local intranasal use. The reluctance of patients and physicians alike to use nose drops is based on results obtained 20 years ago and do not apply to today's medications. Modern investigation has revealed that the ideal intranasal medication should be (a) slightly acid in reaction, (b) buffered to maintain constant pH, (c) isotonic, d) non-irritating and (e) should not interfere with ciliary activities. Such a preparation should produce rapid and effective vasoconstriction without interfering with the normal physiologic mechanisms which aid the nose in its own reactions. In addition, such a preparation should produce little or no rebound congestion and no systemic manifestations(5). The plastic spray containers are more acceptable to children and are more certain in administration should the child be uncooperative. Every parent should be instructed in the proper use of these nasal sprays – the child sits erect, the head is tilted slightly forward, the spray is directed somewhat backward (yet the bottle must be pointed above the horizontal or a spray is not produced) at an angle permitting the medication to pass into the nasal cavity. Two or three vigorous "squirts" should be used every 3 or 4 hours in each nostril, the child being encouraged to sniff between each "squirt" to pull the medication well into the nasal passageway. The nature of the nasal secretions will influence the composition of medication to be used. If the mucus is not discolored nor unusually

thick, preparations such as ephedrine or Neosynephrine are adequate. If allergy is a factor, preparations containing hydrocortisone are particularly valuable. If the discharge is tenacious or discolored, best results are obtained using a preparation containing a detergent, an antibiotic and a decongestant in combination.

To insure that drainage of the sinus cavities is complete, intranasal medication should be continued beyond the time when the cough, the nasal obstruction, the running nose, etc., have disappeared, then discontinued gradually.

EXPECTORANTS:

Thickened, tenacious mucus will drain poorly from the paranasal sinuses. Thinning of the secretions is aided by the administration of one of several preparations. (a) Saturated solution potassium iodide is one of the most convenient to use. A rough guide to dosage is one drop per year of age given t.i.d. with a minimum of 2 or 3 drops t.i.d. (b) Calcium iodide is available in tablet form (Calcidin) or in flavored vehicles (Calcidrine Syrup). (c) Ammonium chloride is commonly employed in various expectorant compounds.

These should be given until all evidence of thickened mucus is gone, then gradually reduced.

ANTI-INFECTIOUS AGENTS:

Even though fever may be absent, if the sinus drainage is thickened, discolored or of long duration, the administration of systemic antibiotics or sulfonamides is beneficial. The complications of sinus drainage (bronchitis, pneumonia, etc.) will, of course, be benefited by antibiotics.

INHALATION THERAPY:

The use of steam inhalation serves to add moisture to the nasal contents and reduces the irritating, drying effect of inspired air to the throat, larynx and bronchi, particularly when the patient is forced to mouth breath. The use of tincture of benzoin, "Vicks," etc. in the water is often irritating.

Steam vaporizers usually employed at home are inadequate even in the smallest room. Partial enclosure of the child's crib or bed by sheets, etc. will multiply the humidifying effects of steam.

More efficient humidification (and without added heat) is afforded by using a continual aerosol of either distilled water or a wetting agent (Alevaire). Gas under pressure, supplied by compressed oxygen or an electric compressor, is passed through a nebulizer such as DeVilbiss No. 841.

Intermittent positive-pressure breathing using the Bennett apparatus has proved a valuable means of introducing medication into the upper and lower respiratory passageways (6, 7). This apparatus employs a mask which fits over the nose and mouth. Under appropriate positive-pressure, a fine aerosol is introduced into the respiratory passageways on inspiration but a sensitive valve interrupts this flow at the onset of expiration. When the nasal passageways are blocked with mucus or edema little of the nebulized medication can reach the sinus cavities since the patient must mouth breathe almost exclusively. After the intranasal spray and expectorants have improved the nasal air exchange, medications can reach the sinuses when the Bennett apparatus is used. However, its greatest benefits are derived from transporting locally effective antibiotics, detergents and broncho-dilators into the lower respiratory tract, comparable to the manner in which the nasal sprays apply medication locally into the nose. Whenever there is evidence, either by the presence of a severe cough, by positive roentgenogram or by auscultation, that the lower bronchial tree contains thickened mucus, the use of the Bennett apparatus may be beneficial. Patients under 5 years of age rarely are capable of cooperating. Treatments are given from one to four times daily as indicated, each treatment lasting 10 to 20 minutes. The positive-pressure may be set at 10 to 20 cm of water pressure depending on the vigor of the patient's expiration. The solution used in the nebulizer should contain a detergent, an antibiotic, and a broncho-dilator. An effective formula is as follows: Alevaire 2 cc, Isuprel ½ cc of a 1:200 solution, neomycin ½ cc of a solution containing 50 mgm per cc.

ANTI-ALLERGIC TREATMENT:

Obstruction of the nasal passageways occurs commonly in allergic conditions and may lead to sinusitis and sinus drainage. Should the allergic condition be severe, allergic investigations and subsequent desensitization may be required.

Antihistamines are valuable in decreasing the nasal swelling and excessive mucus production associated with nasal allergy. However, antihistamines may worsen sinusitis if given without accompanying expectorants and local therapy. One action of antihistamines is to decrease secretion by the mucous glands. If at the onset of treatment the retained sinus secretions are thickened, antihistamines will severe to render them more tenacious.

RADIATION THERAPY:

Radiation therapy, using either radium or x-ray, has been advocated to reduce the hypertrophy of lymphoid tissue commonly associated with sinusitis in children (1, 2). Using x-ray, the average child may require three treatments a week with a maximum of 12 treatments. Beneficial effects on mucosal congestion and lymphoid hypertrophy are apparent two weeks after treatment.

SURGICAL TREATMENT:

Surgical procedures to improve drainage from the paranasal sinuses are rarely necessary in childhood. Likewise, surgical removal of mucosal polyps is seldom required since they usually regress with proper medical treatment or radiation therapy. Hypertrophied adenoid tissue also regresses when postnasal drainage ceases but adenoidectomy is sometimes necessary to remove obstruction. Tonsilar enlargement associated with the sino-bronchial syndrome is a result of postnasal drainage, not a cause, and tonsilectomy does not benefit the sinusitis.

CASES

CASE I – M.F.A., a 12 year old girl, was first seen in my office in August 1955, because of severe pulmonary disease of six months duration diagnosed as fibrocystic disease. She had been in good health, weighed 98 pounds in February 1955, and was attending school regularly. In April 1955, a "cold" began with considerable cough, particularly on awakening in the morning, occasionally accompanied by vomiting. Her cough persisted in spite of medical treatment. By June 1955, she had lost 18 pounds and she was advised to move to a drier climate. However, in Arizona she continued with cough, daily vomiting of mucus, frontal headaches and weight loss to 77 pounds on July 1. Physical examination in August 1955, revealed purulent mucus in the nasal passageways and posterior pharynx. Auscultation of the chest revealed only occasional ronchi. Roentgenogram of the chest disclosed considerable mediastinal widening and prominence of the bronchovascular markings throughout the lungs, more prominent in the dependent portions. Diagnosis was sino-bronchial syndrome and treatment was begun consisting of nasal spray q 3-4 h (Biomydrin); saturated solution potassium iodide, 15 drops t.i.d. oral tetracycline and supportive therapy. Her improvement was rapid. The daily vomiting of mucus ceased within a week. Her appetite improved and within a month she had gained 10 pounds. When last heard from in January 1956, she was in good health.

CASE II – M.H., a 5½ year old boy, was first seen in March 1956, because of a severe cough. Similar pulmonary infections had occurred since one year of age during the winter months, always as part of a "cold." In the six months immediately preceding his first visit, there had been at least one pulmonary infection a month with fever severe enough to require bed-rest and antibiotics. Hospitalization had been resorted to on two occasions. Neither intranasal medication nor expectorants had been prescribed. When examined in March 1956, the nasal passageways contained a purulent yellow discharge. Auscultation of the chest disclosed a few squeaks bilaterally. The temperature was 99.6 orally. Treatment consisted of nasal spray q 3-4 h (Biomydrin-F); saturated solution potassium iodide; 8 drops t.i.d.; penicillin and streptomycin; and supportive therapy. Improvement was rapid; he slept without cough or vomiting the day medication began. His sinus drainage cleared within a week. When last heard from in September 1956, there had been no recurrence of symptoms of the sino-bronchial syndrome.

SUMMARY

1. Sinusitis is common in childhood although frequently overlooked.

2. Drainage of purulent material from the paranasal sinuses implants infection in the lower respiratory tract and is a common cause of recurrent pulmonary infections in children.

3. Unless the sinuses are cleared of retained

secretions, drainage of purulent material may reoccur resulting in repeated infection of the lower respiratory tract.

4. Principles of treatment of the sino-bronchial syndrome are outlined, including intranasal medication, expectorants, antibiotics and aerosol inhalations. The Bennett apparatus affords an excellent means of introducing medication locally into the lower respiratory passageway.

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MONGOLISM AND ACUTE LEUKEMIA

A Case Report

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RECENT reports of the occurrence of leukemia in children suffering from mongolism has focused attention upon these relatively rare disorders. The first case of leukemia in a Mongoloid child was reported by Brewster and Cannon(1) in 1930. Since that time, until this year, no further reports have been made. Krivit and Good(2) report four cases and Marrit and Harris(3) an additional four cases. The normal incidence of Mongolism is said to be about 1 per 500 live births. Leukemia in the below five year age group is said to be about 5/100,000 population. According to Krivit and Good this would give an expected occurrence of leukemia-mongolism in this age group of about 1/10,000,000. Sixteen children diagnosed leukemia have been admitted to Saint Mary's Hospital in the period January 1945 through 1955. One of these, the case to be reported, was a mongoloid child.

The observation of the occurrence of these two disorders directs attention to the time of fetal life when it is believed the development of Mongolism occurs. It is thought that a type of stress is placed on the embryo at sometime between the sixth and ninth weeks of fetal life. Granulocytes are found at the seventh week and lmyphoblasts at the eighth or ninth week. This leads to the possibility that the same stress that produces mongolism may alter the bone marrow with subsequent development of leukemia. Recent studies have extended the concept that leukemia may be transmitted by a filterable agent. This thought leads to further speculation in that the leukemia producing agent may enter the fetus and be responsible for the production of Mongolism. The case to be reported offers nothing new and is reported for statistical reasons primarily and to stimulate speculation about these two tragic conditions and to further emphasize that what may seem to be a remarkable coincidence may be part of a disease pattern.

CASE REPORT:

R. K. male, age 6, admitted to Saint Mary's Hospital January 25, 1955, for a bone marrow aspiration. A complaint of pallor, spontaneous bruises occurring over the body, weakness and fussiness for about two weeks was offered.

The boy had been diagnosed as having Mongolism at birth. The delivery was normal, the mother was a forty year old primipara.

Physically the boy was the classical picture of Mongolism. He was very pale. There were ecchymoses scattered over the body. The tonsils were very large, the gums pale but bleeding could be produced by the lightest pressure. The heart rate was about 120. There was a loud systolic murmur over the left sternum. This was interpreted as indicating an interventricular defect.

The past history was one of many colds, anemia and convulsive attacks occurring with high fever. He had several kinds of medicines including Tridione, and glutamic acid. A blood count done on June 7, 1949 at age 8 months was as follows:

Hemoglobin	13.9
Red Blood Count	4,900,000
Stabs	1
Polymorphonuclears	51
Eosinophiles	0
Basophils	0
Small Lymphocytes	46
Monocytes	2

The blood count of January 25, 1955 reported the following:

Hemoglobin Grams	7.8
Hemoglobin %	56%
Hematocrit	23%
White Blood Count	122,000
Lymphocytes	99%
Metagranulocytes	1
Distintegrated Cells	54 in 100 counted
Platelets	60,000

Sed. Rate — 15 min. — 17; 45 min. — 60; 60 min. — 74.
Coagulation time — 5½ minutes.
Bleeding time more than 15 minutes.

Bone marrow puncture was done by Dr. Louis Hirsch and reported as follows: Bone marrow aspirate unsuccessful insofar as liquid material is concerned. However, cancellous bone is obtained and sectioned. This shows no evidence

of normal hematopoiesis. The marrow spaces are filled with relatively uniform deeply staining cells. Examination of peripheral smear reveals large numbers of blast cells whose origin is not evident.

Diagnosis: Acute leukemia.

The boy was placed on cortisone. This controlled the bleeding. Death occurred February 6, 1955. Autopsy was not done.

The report is made of leukemia occurring in a boy, age 6, who was a victim of Mongolism. The report is made to add to the literature the number of cases of this double tragedy as recent reports indicate that more than just coincidence may be present. Any new approach on either problem is worthy of further study.

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Arizona Seminars

SOME THOUGHTS ON THE TUBERCULOSIS PROBLEM

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PROBABLY more than any other disease, tuberculosis reflects the social and economic well-being of the community. Repeatedly in the course of human history, tuberculosis has waxed and waned. In England, the mortality from pulmonary diseases seems to have been very high around 1650, then to have decreased slowly for many decades before climbing to a new peak some 200 years later. What amounted to a great epidemic of tuberculosis in the nineteenth century was directly related to the hard living and working conditions prevailing in the cities at the beginning of the industrial revolution. Long and strenuous working days, malnutrition, life among fumes, smoke and dust seem sufficient reasons to explain the ravages of tuberculosis among those newly brought into nineteenth-century factories. Within a few decades, millions of individuals raised on farms and in small towns were uprooted and exposed suddenly to the debilitating effects of inhumane employment. The same conditions generally prevailed everywhere in Europe and North America during the first half century of industrialization.

The association of tuberculosis with rapid industrialization can be observed in some parts of the world today. Large-scale migrations from rural areas to urban districts, disruption of ancestral habits and low standards of living are now found in many parts of Latin America and Asia, and indeed may play some role in the high tuberculosis rates of Arizona. Accompanying these population shifts, tuberculosis is following the same fulminating course that was so frequent in Europe and the United States of America in the 1830's, and the death rates are reaching 200-500 per 100,000 in the newly industrialized areas.

Beginning about 100 years ago, there began in Europe and North America a general decline in the tuberculosis death rates. It is a highly interesting fact that this decrease began long before any specific measures had been instituted for the control of the disease; and, indeed, before any scientific basis existed upon which to formulate an effective anti-tuberculosis campaign. The germ theory was not accepted in medical circles until about 1880, and the treatment and segregation of patients in sanatoria only began around 1900. When concerted social and medical efforts to control tuberculosis were instituted at the beginning of this century, the annual mortality caused by the disease in America and England had already fallen to 200 per 100,000, about half the figure that prevailed during the height of the epidemic. While the influence of the anti-tuberculosis campaign during the past 50 years has been and remains immense, it would be unwise to overlook the natural forces that, independent of conscious policies, had begun to alter the balance between the tubercule bacillus and man long before the microbiological era.(1)

It is well-known that tuberculosis mortality quickly increases in countries upset by such major social upheavals as war, famine, or economic depressions. During both World War I and II sharp rises in the mortality curves of tuberculosis occurred among the civil populations of all those countries seriously affected by war conditions. With the return of peace, deaths from tuberculosis again declined rather rapidly to pre-war levels. Recent studies tend to confirm the conclusion that where urban living is accompanied by inadequate or slum housing, low income, deleterious effects of overcrowding and poverty, tuberculosis continues to exist at a higher level of prevalence than in other areas of the same city where the general physical and social environment is more favorable.(2) Indeed the course of tuberculosis in the community has consistently fallen or risen in inverse ratio to the standard of living. Sir William Osler was so impressed by this relationship that he is reported to have said that "tuberculosis is a social disease with medical aspects."

One important factor in the downward trend of tuberculosis in the U.S.A. is directly due to

the activity of health agencies. This is in the field of bovine disease. The practical eradication of bovine tuberculosis was accomplished largely by two measures: the pasteurization of milk supplies; and the elimination of tuberculin-positive cows from dairy herds. With the great reduction in bovine tuberculosis, there has been a sharp diminution in all forms of extra-pulmonary tuberculosis in children with a consequent reduction in death rates.

In the United States from 1900-1916 the rate of decline in the tuberculosis death rate was about 2 per cent per year; after a brief rise coincident with World War I, the decline continued at an accelerated rate, about 4 per cent per year, until around 1946. With the introduction of the new drug therapy which became available on a large scale in 1947, the picture has markedly changed. In the 7-year period between 1947 and 1953, the tuberculosis death rate in the U.S.A. fell from 33 per 100,000 to 12 per 100,000 or an average annual decline of 9 per cent.(3) Along with the downward trend, the shift in age and sex distribution has been striking. In the first decade of the century, infants under 1 year of age had a higher tuberculosis death rate than any other age group. In recent years this group has had a lower death rate than has any of the adult age groups. There has also been a marked change in the ratio of mortality from tuberculosis between the sexes. In 1900, males in the U.S.A. had about the same mortality rate as females, while at present the male rate is about twice as high as the female. As for differences among racial groups, death rates for non-whites are about three times as high as for the white population.

Although a large proportion of all tuberculosis is reported among the younger part of our population, the actual case rates are higher for the older age groups. The mortality rates are marked by a peak during infancy, followed by the lowest morbidity and mortality of the whole life span from 5-10 or 12 years. A second wave of tuberculosis starts with adolescence and reaches a peak in the 20-29 year group. In females, this is followed by a gradual dip in mortality and final rise during the last three decades of life. In males, the mortality rate continues to rise from 30 years of age until the end of life. No longer in this country is tuberculosis primarily a disease of young adults, but rather of middle life and in men of old age.(4)

The decline in tuberculosis has not been uniform across the country. There are variations between states and between rural and urban areas. The death rates are generally high in the large cities. Cities of 100,000 and over have a tuberculosis death rate approximately 80 per cent higher than that of the remainder of the country. In fact, when the death rates of each state exclusive of the large cities are studied, there are only 4 states (Arizona, Arkansas, Kentucky, and Tennessee) which have death rates higher than the average rate for the large cities.(5)

In spite of the splendid achievement of lowering the tuberculosis mortality rate in the U.S.A. from 199 per 100,000 to the low national rate of 10.6 per 100,000 in 1954, there are still some 15,000 Americans dying annually from the disease, many of them in the prime of life. Some 500,000 cases are currently known to health departments in the U.S.A., about half of these being in the active stage. In addition, it is estimated that there are some 700,000 unknown cases in this country of which some 150,000 are thought to be active.(6)

Epidemiologists in studying the tuberculosis situation in a given area mainly use 3 yard sticks: (1) mortality rate, usually expressed as the number of deaths a year per 100,000 population; (2) morbidity rate, i. e., number of cases reported a year per 100,000 population; and (3) tuberculin surveys to determine the prevalence of infection. Deaths measure only one aspect of the effect of tuberculosis upon the population. The death rate has never been a precise index of the trend of tuberculosis in the community; and now, due to the effectiveness of the new drugs in the treatment of the disease, its usefulness is more limited than ever. In most civilized countries, deaths are well reported to the authorities, so mortality as an index of trends is still very useful as an indication of the relative effects of tuberculosis on various population groups.

Morbidity rates in this country now offer a good index of the trend of tuberculosis, although even a decade ago reporting of new cases was so inadequate in many places as

to make this measure almost useless. The degree to which physicians report new cases still varies among the states. In 1952, the ratio of cases to deaths varied between states from 2.9 to 10.7. From 1910-1940, the trends of reported morbidity and mortality were essentially parallel, but from 1940-1947, the death rate declined by 27 per cent, while the number of known cases increased in proportion.(7) Fortunately, the tide seems to be turning, and there has been in recent years approximately a 3 per cent decline in the number of new cases reported per year.(5) Tuberculosis case finding and reporting now are definitely superior to that of previous decades. Some 15½ millions of individuals had X-ray examinations of the chest in 1953 in the U.S.A. in case-finding surveys. That was 2 million more than in 1952. Of the total new cases reported in 1953, 32 per cent were first discovered as a result of case-finding X-ray surveys.(8)

In tuberculosis, infection is not synonomous with disease. It has been estimated that while about 50 per cent of the adult American population may have at some time been infected with the tuberculin bacillus, only 3-5 per cent ever develop active disease.(4) Development of tuberculosis in man is a biological struggle between the invasive powers of the agent and the resistance of the individual, modified by a variety of environmental factors. The steadily declining death and sickness rates from tuberculosis in this country indicate that the balance has been in favor of the human host. One can readily see, however, from recent European war experience that the balance is only too easily reversible.

Tuberculin testing of population groups has been done over a considerable period of years on a wide scale; yet differences in materials, dosage, technique, and the failure to persist in continued long-term testing programs have limited the value of the information obtainable from their study. Some observations can be made however. First, there are marked differences in the number of reactors between areas and population groups. In crowded environments having a high tuberculosis death rate, the rise in percentage of reactors with age is faster. And, second, the age-specific prevalence of infection appears to have declined in recent years in many localities. In Massachusetts, the percentage of positive reactors among grade-school children dropped as follows: 1924 – 28 per cent; 1939 – 14 per cent; and 1955 – 2 per cent.(4) Teague has given the following figures for the percentage of positive reactors among high-school children in Philadelphia: 1929 – 84 per cent; 1939 – 43 per cent; and 1949 – 16 per cent.(9)

Recently a single-dose standardized tuberculin test employing a more refined preparation, Purified Protein Derivative (PPD), has been recommended for general use by the World Health Organization and the National Tuberculosis Association. Using this test, a study was carried out on a large number of U. S. Naval recruits ranging from 17-21 years of age at the San Diego Base.(10) Some of the results of this study are summarized in Table I in which is given the percentage of positive reactors residing in selected states together with the average tuberculosis death rates in the white population of those states for the period 1939-1941 (mid-point of the lives of the men tested).

Examination of this table reveals that states with low tuberculosis death rates also have low percentages of tuberculin reactors in the 17-21 year group. It will also be seen that Arizona has the highest percentage of reactors, as would be expected from its high tuberculosis mortality rates for the period given.

It would appear that in this country exposure to the tubercule bacillus has been decreased and on the whole postponed. In many communities, the results of repeated tuberculin surveys, carefully standardized and well planned, may well be the best yardstick of the tuberculosis problem. For pinpointing special situations where infection rates are still high and where energetic control measures are needed, the tuberculin test is of unqustioned value.

Arizona leads all the states in the severity of the tuberculosis problem. For many years, Arizona has headed the state list of mortality rates and rates for new cases reported. It is reassuring that the death rate from tuberculosis in Arizona has been steadily declining for many years and is now approximately at the point reached by the national rate around 1949.

In Table II, Arizona's tuberculosis death rates are compared with those of the registration area of the U.S.A. for selected years from 1930-

1954. It will be seen that both in Arizona and in the nation at large, there has been a steady decline in these death rates over this 25-year period. From this table, one can appreciate the remarkable decline in total annual tuberculosis deaths in Arizona during this period when the population was growing rapidly. These data point up again the great preponderance of tuberculosis deaths among the males in the white population and among the non-whites in the total population.

In Table III are summarized the tuberculosis deaths among Arizona residents in the 4-year period, 1951-1954, arranged by race, sex, and age. Several points of interest are apparent from these data. Among the white population only 22 or 2.2 per cent of deaths occurred in children under 5 years of age, among non-whites the figures are 81 deaths or 22.5 per cent. This is porbably an indication of the intensity of exposure to infection in non-white households. Among white males 531 or 74.6 per cent died at 45 years or over, while only 110 or 47.6 per cent of deaths in females were in these same age groups. As has been reported in the national picture, the Arizona statistics show tuberculosis mortality among white males occurs approximately three times more frequently than in white females. This difference in mortality between the sexes is not marked among the non-white population.

Several explanations are usually given for the high tuberculosis rates in Arizona. Hundreds and perhaps thousands of sufferers from the disease were sent over the years from other states to seek the favorable effects of the arid sunny climate of the southwest. This migration of patients to the state still persists, although perhaps at a lower level than formerly. The introduction of effective drugs in the late 1940's gives more promise for successful therapy at home and will undoubtedly reduce the number of patients seeking the benefits of climate. In 1952-1953, of the 708 individuals reported as dying with tuberculosis in Arizona, 102 or 14.4 per cent were non-residents of the state. In Table IV are summarized the data for tuberculosis deaths occurring among Arizona residents for 1951, 1952, and 1953 by length of residence in the state. (Data given for white population only.) It will be seen that of the total 714 deaths with the data available, 190 or 26.6 per cent of the individuals had resided in the state for less than 5 years. During that period, only 16 deaths from tuberculosis were reported among children under 5 years of age. This suggests that most of those individuals came to Arizona already suffering with the disease.

Another factor in the high tuberculosis rates in Arizona is the racial composition of the state's population. Through rapid elimination of the more susceptible human strains, races having a long and intimate association with tuberculosis develop a certain amount of racial resistance. Such resistance, developed on the basis of natural selection, is not sufficient to offset unusually unfavorable living conditions, as shown by the heavy toll taken by the disease in India, Egypt, and China. In Table V, the 1950 census figures for Arizona showing the racial composition of the state's population are given.

The great susceptibility of the American Indian to tuberculosis is so well-known that it scarcely requires any further comment. It is worthy of note that of the 1,062 deaths reported from tuberculosis in Arizona for the 3-year period 1951-1953, 252 occurred among Indians. This figure amounts to 23.7 per cent of the total, although the Indian population of the state is less than 10 per cent of the whole.

Another indication of the greater severity of tuberculosis among the Indians is that in 1951 deaths due to tuberculosis represented 11.9 per cent of all Indian fatalities while among the white population tuberculosis caused only 5.3 per cent of the total deaths. In 1953, these figures were 7.2 per cent for the Indians and 3.1 per cent for the whites.

Aronson recently published encouraging data demonstrating a decline in the number of positive reactors over a period of years among the children of Indians on the Pima and Apache Reservations in Arizona.(12) These data are summarized in Table VI. It will be seen that among children in the 5-9 year age group there has been quite a significant decline in the number of tuberculin positives during the period between the two surveys. This decline is less marked among the 10-14 year group and among the children aged from 15-19 years. It is to be hoped that more favorable economic con-

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[1]Posner, A. C., *et al.*: Further Observations on the Use of Tetracycline Hydrochloride in Prophylaxis and Treatment of Obstetric Infections, *Antibiotics Annual* 1954-55, pp. 594-598.

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TABLE I*

PERCENTAGE OF POSITIVE REACTORS TO TUBERCULIN AMONG U. S. NAVY RECRUITS 17-21 YEARS OF AGE BY STATE OF RESIDENCE TOGETHER WITH AVERAGE ANNUAL TUBERCULOSIS DEATH RATES (WHITE POPULATION ONLY) FOR THE YEARS 1939-1941 (MID-POINT IN THE LIVES OF THE RECRUITS)

State	Number Tested	Per cent Positive	Tuberculosis Death Rate
Arizona	472	22.7	150
New Mexico	601	18.0	72
California	8,496	11.6	51
Texas	6,834	8.7	55
Colorado	1,444	8.2	51
Kansas	1,900	6.2	21
Iowa	2,567	4.9	16
Utah	976	4.4	14

*Taken from: Palmer et al, Public Health Reports, 1956, 71, 633-645.

TABLE II*

TUBERCULOSIS DEATHS IN ARIZONA FOR SELECTED YEARS FROM 1930-1954 BY RACE AND SEX TOGETHER WITH TUBERCULOSIS DEATH RATES** FOR ARIZONA AND FOR THE UNITED STATES REGISTRATION AREA FOR THE SAME YEARS

Year	Arizona							United States #
	Estimated Civilian Population	Tuberculosis Deaths					TB Death Rate	TB Death Rate
		Total Number	White		Non-White			
			Male	Female	Male	Female		
1930	435,573	1,441a	978		463		330.8	74.5
1940	449,261	846	622		224		188.3	45.9
1945	589,221	776	410	170	108	88	131.7	39.3
1950	747,000	447b	215	82	74	76	59.8	21.7
1951	772,000	427	231	74	71	51	55.3	19.3
1952	825,000	361	189	62	58	52	43.7	15.0
1953	876,000	274	149	48	41	36	31.3	11.6
1954	909,000	241	143	47	29	22	26.5	10.6

*Data from Vital Statistics of the United States, National Office of Vital Statistics and from Arizona State Department of Health Reports.

**Number of deaths per 100,000 of population for the year.

Age specific Death Rates for States in Registration Area.

a Deaths by place of occurrence.

b Deaths by place of residence (1950-1954).

TABLE III*

TUBERCULOSIS DEATHS IN ARIZONA RESIDENTSFOR THE YEARS 1951, 1952, 1953, AND 1954 BY RACE, SEX, AND AGE

Age Groups by Years	Tuberculosis Deaths					
	White			Non-White		
	Total	Male	Female	Total	Male	Female
Under 1 year	4	3	1	29	16	13
1 - 4	17	9	8	52	25	27
5 - 14	5	3	2	23	12	11
15 - 24	27	12	15	59	27	32
25 - 34	102	60	42	50	25	25
35 - 44	147	94	53	37	17	20
45 - 54	223	172	51	33	21	12
55 - 64	227	202	25	21	16	5
65 - 74	128	106	22	26	18	8
75 and over	61	50	11	29	21	8
Unknown	2	1	1	1	1	0
Totals	943	712	231	360	199	161

*Data from National Office of Vital Statistics, Washington, D. C., and from the Annual Reports of the Arizona State Department of Health.

ditions and the recent move to supply better educational and medical facilities to the Indian population will serve to speed up this decline in their tuberculosis infection rates.

In the 1940 and 1950 census reports persons of Mexican birth or ancestry, who were not definitely Indian or of another non-white race, were classified as white. It is not easy, therefore, to get recent figures on the susceptibility of that group to tuberculosis in Arizona. In 1946, however, 15.3 per cent of all tuberculosis deaths in the state were reported among the Mexican element of the population. This would indicate a high degree of susceptibility, which is not surprising as many of the Mexican people coming to this state are from rural areas where there is likely to be a lower incidence of tuberculosis than in the towns of Arizona.

It is also well-known that the American Negro is highly susceptible to tuberculosis. Although only 3.5 per cent of Arizona's population according to the 1950 census is classified as Negro, indications are that this group has a disproportionately high tuberculosis rate. Fortunately, the decline in deaths and illness from tuberculosis among the white population is being fully shared by the non-whites.

Possibly there are other less apparent reasons why Arizona's tuberculosis rates are high. Cer-

TABLE IV*

TUBERCULOSIS DEATHS ACCORDING TO LENGTH OF RESIDENCE IN ARIZONA (WHITE RESIDENTS ONLY) – 1951, 1952 AND 1953

Total Tuberculosis Deaths	Length of Residence in Arizona					
	Less than 1 year	1 - 4 years	5 - 9 years	10 years and over	Life	Not Reported
751	42	148	155	297	72	37

*Data for this Table derived from Statistical Supplements to Annual Reports of the Arizona State Department of Health.

TABLE V*

ARIZONA – 1950 CENSUS OF POPULATION

Population	Total	White		Indian	Negro	Other***
		Native Born	Foreign** Born			
Percentage of State's Total	100	81.2	6.1	8.8	3.5	0.5
Actual Count	749.587	608.917	45.594	65.761	25.974	3,341

*Data taken from U. S. Census of Population: 1950 Bureau of the Census.

**Of the foreign-born white population, 24,917 were born in Mexico.

***Mostly Chinese and Japanese.

TABLE VI*

PERCENTAGE OF POSITIVE REACTORS TO TUBERCULIN (P. P. D.) AMONG INDIAN CHILDREN ON RESERVATIONS IN ARIZONA IN TWO SURVEYS

Reservation and Tribe	Age Group by Years	Date of Survey		
		1936 - 1937	1940 - 1941	1954
Pima	5 - 9	23.4		7.9
Apache - San Carlos			29.3	8.3
Apache - Fort Apache			49.2	19.5
Pima	10 - 14	46.2		43.2
Apache - San Carlos			53.4	40.8
Apache - Fort Apache			78.0	53.7
Pima	15 - 19	78.2		70.9
Apache - San Carlos			79.9	69.6
Apache - Fort Apache			94.8	83.4

*Data taken from Aronson and Taylor, Amer. Review of Tuberculosis, 1955, 72, 35 - 52.

tainly social and economic factors are important. As Winslow so wisely stated in a recent editorial, "The tubercle bacillus is not **the** cause of tuberculosis. It is a cause of the disease."(11) More study must be given to determine the possible significance of the other factors in Arizona.

In contrast to the falling mortality rates for tuberculosis in Arizona, there has been no comparable decline in the number of new cases being reported each year. This is partly explained by a greater interest on the part of physicians in reporting their cases to the health department, but is more likely due to the increased efficiency in case-finding measures. It is possible, too, that patients with tuberculosis are less reluctant to seek medical care, now that effective drugs for treating the disease are available. At any rate, the continued high incidence of active cases in the population indicates that the tuberculosis problem is still of major importance to the community.

CONTROL MEASURES

Perhaps the most effective way of reducing the incidence of tuberculosis in the community is the general improvement in the economic and social welfare of the people. This, of course, is most difficult and is not directly the responsibility of the physician or the health officer. Efforts can be made to eliminate substandard housing with its attendant ill-effects. Attention to improvement of nutrition through health education and through school lunch programs may also prove highly beneficial in promoting disease resistance among children.

Specific measures aimed at the control of tuberculosis should be directed toward early diagnosis, adequate treatment, prevention of spread of infection, enhancement of resistance, rehabilitation of patients, and education of the public as to the natural history and dangers of the disease.(13)

Private physicians have an important part to play in the early diagnosis of the disease, in the education of the patient, in the medical care of patients, and in reporting the cases promptly. It is the duty of the attending physician to persuade the patient to undergo prompt and adequate treatment and to ascertain that household and other intimate contacts of the patient are brought in for X-ray examination of the chest.

Under the treatment regimes made possible by the newer drugs, patients are often released from the hospital for continued care in the home. The responsibility of the physician in such cases is to guard against relapse. In the U.S.A., relapses are reported in about 115,000 cases per year. An increase in the number of these relapses began about 1948 shortly after the beginning of the chemotherapeutic era.(14) It would appear that many "incomplete cures" have resulted from inexpert handling of the new drugs. Patients with active disease treated by trained sanatorium physicians generally do well. Those inadequately treated outside of sanatoria may develop chronic disease due to "drug resistant" bacilli.

The health officer has the chief responsibility for tuberculosis control in the community. In addition to maintaining an accurate up-to-date record of all cases in his area of jurisdiction, he must assist the private physician in arranging for the examination of all family contacts and in keeping patients under proper medical supervision. Periodic examination of sputum from all patients suspcted of having active tuberculosis is highly important to determine whether isolation is needed. The public health laboratory should render expert assistance to physicians and clinics in the examination of sputum by smear, culture, or animal inoculation.

More and more as the prevalence of tuberculosis decreases in the community, the employment of the epidemiological skills of health officers will be required to uncover sources of infection of individual new cases. In many communities cases of tuberculosis are becoming infrequent, so that the disease exists in relatively small household, neighborhood, or occupational epidemics. The contracts of every new case in such areas will have to be investigated with the same care as would be given to a case of smallpox or diphtheria.

Since tuberculosis is especially prevalent among the indigent and medically indigent, many patients are unable to pay for private medical care. It is the duty of the health department to provide clinic facilities at convenient times and places to supply diagnostic and treatment facilities for this important segment of the population. The fact that treat-

ment can now be given in the home and in the hospital has lightened the load of the institutions, but almost correspondingly increased that of clinics. Public clinics instead of being largely limited as in the past to diagnosis of suspects or follow up of discharged hospital cases, now often have a heavy load of patients under drug therapy. New York City Department of Health clinics had 4,412 such patients at the end of 1955; in fact, a greater number than the 3,568 patients in the institutions of the Department of Hospitals. Likewise, the Chicago Municipal Sanatarium had more patients at the end of last year under drug therapy in their clinics than in the hospital services.(15) Home-care programs are particularly important for the treatment of newly discovered cases faced with long waiting periods for hospitalization, as well as for the continuation of care for those discharged from sanatoria.

It will be readily appreciated that in such a medical-care program the welfare department must play an important role. In addition to determination of ability to pay for necessary care, the welfare department must determine and furnish reasonable assistance to provide for the support of the patient's dependents during the period he is unable to work.

Voluntary agencies, particularly the local Tuberculosis and Health Association, also fulfill an important function in the anti-tuberculosis campaign. The especial role of this organization is education of the public about protection against tuberculosis and cooperation with the medical society and the health department in the elaboration of a satisfactory community program.

As already indicated, the success of the new anti-tuberculosis drugs has markedly altered the picture in a favorable direction. Some of the immediate practical benefits may be listed as follows: 1. A great reduction in toxic symptoms and a corresponding improvement in well-being and morale of the patient. 2. A decreasing necessity for prolonged rest in bed. 3. Rapid preparation for necessary surgery and a great reduction in surgical risk. 4. A rapid decrease in cough and expectoration and conversion of sputum from positive to negative. 5. The prevention or cure of lethal forms of the disease in infancy and early childhood. 6. A reduction in the number of spreaders of infection by the cure of early tuberculosis before it becomes advanced disease.(14) It will be appreciated that these effects are of considerable public health importance.

Probably the most effective method for the discovery of new cases of tuberculosis in the community is the mass X-ray survey. To be done properly, these surveys must be preceded by an educational campaign, and followed by careful, competent, and long-continued observation of those cases discovered. Every effort should be made to examine population groups in which there is reason to suspect a high incidence of tuberculosis, especially males in the older age groups. Industrial workers, pregnant women, relief recipients, and inmates of institutions ought to be examined. Routine X-raying of all persons admitted to general hospitals for any cause has also been shown to reveal many unsuspected cases of tuberculosis. Among younger age groups in the population, it is frankly wasteful nowadays to examine them by X-ray without prior tuberculin testing to eliminate the large number not even infected.

By 1945, a case-finding program using a mobile photofluographic X-ray unit has been initiated by the Arizona State Department of Health. Up to the present, something over 700,000 chest X-ray examinations have been made in this state. The most impressive survey was carried out in Maricopa County in 1951 with the cooperation of a team from the U. S. Public Health Service. In the course of this survey, chest X-ray examinations with small films were done on 164,445 residents of Maricopa County. Of this number, 9,080 were classified as tuberculosis suspects. Of those who returned for large X-ray films of the chest and other diagnostic studies, 3,065 were finally classified as tuberculosis. From this number, 201 active tuberculosis cases which never before had been diagnosed were notified to the health authorities. In addition to this valuable result, this survey gave a strong indication of the grave nature of the tuberculosis problem in Maricopa County.(16)

To determine the progress being made in the control program, all available measuring methods should be utilized efficiently; i. e., (1) more complete and more accurate reporting of cases and deaths from tuberculosis, (2) the

setting up of long-continued, standardized tuberculin testing surveys in selected areas of the state to determine the extent to which infection levels are changing among the younger age groups of the population, and (3) the increased use of mass X-ray surveys to uncover previously unknown latent and active cases.

To provide treatment for active cases, the community must have available an adequate number of beds in institutions equipped and staffed to render a good quality of medical services. In general, the tuberculosis sanatorium serves three functions: as an isolation hospital; a treatment center; and a training school, where the patient is taught how to get well, how to remain well, and how to protect others from his disease.

In 1952, the Division of Hospital Facilities of the U. S. Public Health Service estimated that to meet the standards set up under the Hospital Survey and Construction Act (Hill-Burton Act) (i. e., 2.5 beds times the average annual number of tuberculosis deaths over the most recent 5-year period), an addition of 872 new beds for tuberculosis patients would be required in Arizona. At present, due to falling death rates, this number would no doubt be considerably smaller, but the need for new hospital facilities is still urgent. To help alleviate the shortage of beds, more consideration should be given to increasing the number of beds for tuberculous patients in general hospitals.

Rehabilitation of the patient so that he may resume useful employment is assuming an ever-increasing importance in the management of the tuberculosis problem. Often assistance is required for the patient in finding an occupation which he can safely pursue when he has recovered. Such aid may be crucial in preventing a serious relapse of his tuberculosis.

In 1955, the Arizona Legislature passed a Tuberculosis Control Act which is intended to strengthen the health departments in hastening the downward trend of that disease in this state. While this Act is not all that might be desired, it should assist materially in securing proper treatment for many patients who otherwise might have remained a dangerous source of infection in the household and to the community. Actually under the provisions of the law, the local boards of health through the board of supervisors of the county shall be responsible for securing care and treatment for tuberculosis persons in an institution or at home. The Act provides funds ($325,000) to the State Department of Health to reimburse the counties for a part of the cost incurred in accomplishing this. An additional amount ($75,000) has been appropriated for the State Department of Welfare to provide adequate support for the dependents of indigent persons who may be hospitalized under provisions of the Act and to provide drugs or other required items for individuals who have been approved for home care.

Even a cursory examination of this program for tuberculosis control will make evident that a goodly staff of well-trained public health nurses and social workers, as well as other auxiliary personnel, will be required for its successful implementation. Unfortunately, Arizona is still lagging behind in public health facilities and in trained health personnel. Until these deficiencies are to some extent corrected, progress in the fight against tuberculosis is likely to be less satisfactory than need be.

SUMMARY

There has been a steady decline in the toll of tuberculosis among the American population for many decades. This decrease, especially in the tuberculosis death rate, is proceeding much more rapidly in recent years. Unfortunately, the number of new cases reported each year has not fallen at the same rate.

Tuberculosis deaths among females have decreased at a more rapid rate than among males, so that the tuberculosis death rates for males are from 2.5 to 3.0 times those for females. There is also a marked difference in the mortality rates by age groups, for females the peak being among the 20-29 year group, and for males the rate continues to rise from age 30 years until the end of life. Tuberculosis also takes a far heavier toll among the non-white segment of the population than in the white.

The importance of social and economic factors in influencing the trend of tuberculosis in the community is discussed. It appears quite likely that the general improvement in living standards, working conditions, and in nutrition in this country during the past century has been of

great importance in accounting for the marked decline in tuberculosis.

Some factors responsible for Arizona's high tuberculosis rates are set forth. Figures are given to show that both the white and non-white segments of Arizona's population are sharing in the general improvement of the national tuberculosis picture. Arizona's tuberculosis death rate is now about equal to that for the nation in 1949.

General and specific measures for the control of tuberculosis are outlined. Arizona's deficiency in public health facilities and personnel needed for the rapid control of tuberculosis is pointed out.

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PHOENIX *Clinical* CLUB

The Case History in this discussion is selected from the Case Records of the Massachusetts General Hospital, and reprinted from the New England Journal of Medicine. The discussant under Differential Diagnosis is a member of the staff of the Massachusetts General Hospital. The other discussants are members of the Phoenix Clinical Club.

MASSACHUSETTS GENERAL HOSPITAL

A FIFTEEN-year-old-girl was admitted to the hospital because of "fainting spells."

The patient had been in good health until she was about five years of age, when a diagnosis of rheumatic fever was made. She was hospitalized for a year and examined annually thereafter, without evidence of recurrence or the development of murmurs. She entered school at the age of seven, and in the next few years cyanosis of the lips and nail beds gradually developed. Although she was moderately active during this time she became short of breath, tired easily and was unable to keep up with the activities of her playmates. Five years before admission she experienced her first syncopal attack, which occurred while she was recuperating from an appendectomy, and was asked by a nurse to sit up. She had suffered similar attacks about every two or three months since then, and these seemed to be related to overexertion and emotional upsets such as arguments with the family. They also came on when she "read too long", and were usually followed by a throbbing headache, chiefly over the vertex, that was relieved by lying down or sleeping. Six months before entry the family moved to another state, and the patient had considerable difficulty adjusting herself to the new surroundings, particularly to her school work. Since that time she had experienced increasing exertional dsypnea accompanied by cyanosis, frequent headaches and weakness in the legs. Fainting spells now occurred about once each day. She became dyspneic on climbing only a few stairs, and fainted when walking up two flights. Three weeks before examination her mother was hospitalized for a major operation, and during this time the patient had only one fainting spell.

There was no history of orthopnea, paroxysmal nocturnal dyspnea or peripheral edema. During the two months before admission she had lost ten pounds in weight.

Physical examination showed a well developed girl in no distress. There was cyanosis of the face, lips and nail beds, and clubbing of the fingers. The eyes were normal. The lungs were clear. The point of maximum impulse of the heart was felt in the midclavicular line. There were no thrills. The pulmonic second sound was very loud and inconstantly split, and its impulse was easily palapable. There were two heart sounds in systole in the pulmonary area. No murmurs were heard. The rest of the examination was negative.

The temperature was 99°F., the pulse 100, and the respirations 20. The blood pressure was 105 systolic, 80 diastolic, in the right arm, 110 systolic, 75 diastolic, in the left arm and 120 systolic, ? diastolic, in the right leg.

Examination of the blood revealed a hemoglobin of 17.7 gm. per 100 cc. and a white-cell count of 11,900, with a normal differential. The hematocrit was 61.5 per cent. In a roentgenogram of the chest the heart was not enlarged, but the main pulmonary artery appeared prominent. The right ventricle appeared to be slightly enlarged on a lateral view. The lungs were normal. An electrocardiogram disclosed a sinus arrhythmia at a rate of 65 per minute and right-axis deviation. The PR interval was 0.14 second, and the QRS interval 0.08 second. The P waves appeared normal. There was a small Q wave with tall R waves and inverted T waves in Lead V_1. The R waves were prominent in Lead V_2. On the fifth hospital day an arm-to-tongue circulation-time determination was carried out; 1 cc. of Decholin was injected on two occasions, one minute apart. A good end point was achieved each time at seven and eight seconds respectively. About five or ten minutes after the injection the patient became markedly dyspneic and restless, and more cyanotic than usual. A short while later she became unresponsive and had a brief generalized tonic-clonic convulsion, followed by a period of apnea. The pulse was 70 per minute, and the blood pressure 180 systolic, 120 diastolic. Respirations were restored for a short time after artificial respirations but soon failed, along with the pulse. Intravenous administration of calcium chloride, intravenous and intracardiac administration of epinephrine, cardiac massage and electrocardiac stimulation were to

no avail, and the patient was pronounced dead about forty-five minutes after the onset of the acute episode.

DR. PALMER DYSART

Paroxysmal dsypnea, syncope, weakness, cyanosis and clubbing of the fingers occurring in a young girl are sufficient to make a diagnosis of congenital heart disease. To further corrobrate this, a marked polycythemia was present. There was hypertrophy of the right ventricle, shown by x-ray which produced a right axis deviation on EKG and there was also prominence of the pulmonary artery, and the abnormally loud pulmonic second sound which was inconstantly split were evidence of increased pulmonary arterial pressure.

Cyanosis and the absence of an audible murmur would seem to rule out several of the most common of congenital heart lesions. Patient ductus arteriosus, with its characteristic machine-like murmur, is an example. This lesion, although considered to be common, is actually comparatively rare as a solitary lesion, for about two thirds of such defects are associated with other congenital cardiac lesions. So, although patent ductus arteriosus, per se, is not classed with the cyanosis producing lesions, it can be associated with those which are.

Due to the absence of a murmur and cyanosis, it was not regonized that a congenital heart lesion was present, when at the age of five, this child was hospitalized for a year with what was diagnosed as rheumatic fever. The basis for this diagnosis is not known, but it is probable that evidence of arthritis was present. The newer testing tools, such as antistreptolysin-O and C-reactive protein were undeveloped then, and it is possible, if ten years before the death of this child placed the episode of rheumatic fever at, or soon after 1945 when penicillin became available, that this antibiotic may have been used, for it was tried extensively as a treatment for rheumatic fever. If such was the case, it may have been indeed fortunate, for penicillin has succeeded in curing bacterial endocarditis, and it is possible that this was the infectious process suffered by this youngster at the age of five, since it is a very common complicating condition in all congenital heart lesions, death being due directly to bacterial endocarditis in 40% of such cases. However, in one condition, interatrial septal defect, a superimposed rheumatic infection is a frequent complication and bacterial endocarditis is rare.

It was several years after this rheumatic fever that the gradual development of cyanosis and dyspnea upon exertion developed, and in the absence of evidence of valvular lesions to substantiate the diagnosis of a progressive rheumatic heart disease, it is evident that this episode complicated and aggravated a pre-existing condition, which, until that time, was not evident. This chain of events would indicate that the congenital heart disease which then became apparent would fall into the class of Transient or Delayed Cyanosis. In this category, an arterial-venus shunt is present, but there is no cyanosis unless circumstances arise which raise the pressure in the right side of the heart, when transient or terminal reversal of flow occurs, with venous blood entering the arterial stream. Included in this group are patent ductus arteriosus, defect of the aortic septum, defect of the auricular septum, patent foramen ovale, and defect of the ventricular septum. Defects of the atrial or ventricular septa are usually associated with pulmonary stenosis, or with defects in the other septum, or all three, or a combination of these with patent ductus arteriosus. Single lesions are rare, occurring in approximately only one-tenth of the cases. A patent foramen ovale, unless quite large or associated with other abnormalities is seldom of any clinical significance, with one exception that is noted, which is that this condition is more frequently associated with embolism than with endocarditis as the cause of death.

Lesions which do not result in the mixing of venous with peripheral arterial blood such as coarctation of the aorta and stenosis of the pulmonary artery are not placed in the Cyanotic Group, but here it is a question of degree, and whether there are coincidental anomalies which do permit usch mixing. A lesion which permits flow of arterial blood into the pulmonic circulation does not of itself produce cyanosis, but, by overloading the pulmonary circulation, can produce right heart failure.

Frequent combinations of defects are classified as entities such as Tetralogy of Fallot, Lutembacher's syndrome, and Eisenmenger's Complex. Without careful and intensive circulation studies with cardiac catheterization and other methods, it is impossible to evaluate the lesions of congenital heart disease. Such studies

were just begun, with arm-to-tongue circulation tests with Decholin when this patient collapsed and died. The circulation times of these two tests were seven and eight seconds. The normal range for the Decholin test is 8 to 14 seconds with an average time of 10 seconds, so the tests would indicate a venous-arterial shunt. These include defects in atrial, inter-ventricular and aortic septa.

Shunts with a high pressure differential such as ventricular and aortic septal defects are noted for the loud systolic and sometimes, diastolic murmurs. Since no murmur was noted, it seems more probable that an atrial septal defect or patent foramen ovale was present, which, because of the lower pressure differential, could be expected to be less certain of being accompanied by an audible murmur. However, in other anomalies such as Eisenmenger's Complex, in which there is a high inter-ventricular septal defect and a shift of the aorta to the right, although diastolic murmurs may be heard at the apex, and pulmonic areas, they are not necessarily present. Another condition in which murmurs may be absent, consists of anomalous pulmonary veins opening into the right auricle, coronary sinus or venae cavae accompanied by a patent foramen ovale. Symptoms may be mild and intermittent in this condition. Uncomplicated inter-ventricular septal defect (Maladie de Roger) also tends to run a symptomless course without cyanosis and with a systolic thrill in one-third of the cases.

Explanation of the mechanism of the production of heart sounds is an intriguing subject, and involves study of the physical properties of matter, the vibrating object, the transmitting medium, standing waves, traveling waves, enforcement, interference, resonance, phase, frequency, pitch, volume, loudness, quality, receptor response, physiology of hearing including Fletcher-Munson Effect, etc. — one topic leading on to another.

Rouanet made the distinction between heart sounds which has become ineradicably custom sanctioned, distinguishing the sound of valve closure at the beginning and end of systole as a heart or arterial tone as opposed to a murmur, a differentiation which is entirely unjustified in a purely physical sense, since both are the result of irregular sonorous vibrations and that of a murmur being more rhythmic upon sound analysis than the mis-named heart tones. Both types of heart sounds are produced by vibrations of the muscular or membranous structures, not by their fluid contents, the difference being in the suddenness of onset and ending of the tone as compared to the gradual beginning and uncertain termination of the murmur.

Timing, pitch, loudness and quality of the various heart sounds depend then upon distance from the listening point, structure of the related parts of the heart and great vessels, differential pressures between chambers, and between chambers and vessels. Abnormalities in structure, both anatomically and pathologically result in alteration of customarily experienced sounds, as noted with a split second sound which is produced by asynchronous aortic and pulmonic closure. While not quite synchronous, these are separated, normally, by two short a time interval to be auditorially appreciable as separate sounds, but, when pathologically, the normal differences are exaggerated, a split second sound is noted, a condition which is more readily appreciable if the first element is the weaker of the two. This last point explains why a split second sound is noted more often in increased pulmonary arterial pressure than in peripheral arterial hypertension, for the weaker first element due to pulmonic valve closure is more readily heard than it is as a second element, when it is overshadowed by the louder first element of aortic valve closure. The pulmonic second sound is normally louder up to 25 or 30 years of age, and this is noted in 90% of all children under 10 years of age, and in about 10% of these, a splitting of the second sound can be recognized.

Until recent years, congenital lesions of the heart, which, according to 1925 statistics comprised from 0.7 to 2% of all cases of organic heart disease, were of pathological interest only. The duration of life and the disability produced depended upon the type and degree of abnormality and its effect upon the circulation. However, with the development of new techniques permitting surgical repair, practical interest and case finding has developed so that by 1950 to 1953 the reported incidence had risen to 7 to 8%. By 1940, the only defect which had been corrected surgically with any success was patent ductus arteriosus, by ligation. Then, anastomotic procedures were developed to be followed by intra-cardiac defect repair under

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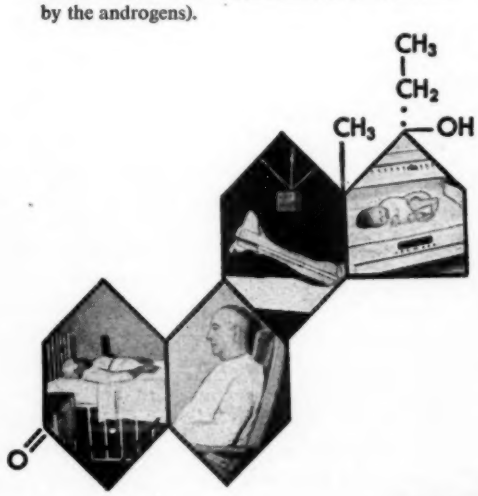

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SEARLE

direct vision under hypothermia with cross-circulation and then biological and artifical oxygenators. It is anticipated that techniques will be developed which will allow the patient's own pulmonary vessels to be cannulated and their own lungs used as oxygenators. As a result of these advances, medical literature is accumulating enlarging series of successful surgical correction of anomalies hither considered to be hopeless. As evidence of this, it is interesting to note that last September at a Symposium on Arteriosclerosis, the University of Minnesota Medical School reported a series of 77 direct vision intra-cardiac operations, and by December, according to their latest report, this number has been raised to 101.

Experience is being gained not only in surgical techniques, but in the ancillary services. For example, prevention of ventricular fibrillation during hypothermia was aided by adding 5% carbon dioxide to oxygen preventing respiratory alkalosis. Neostigmine intravenously and infiltration of the S-A node with xylocaine also provided protection against ventricular fibrillation.

To assist in the evaluation of surgical risk, it has been noted that the mortality rate was 7% with pulmonary artery pressures 70% or less of systemic, and about 55% if the pulmonary artery pressures were above 70% of systemic arterial pressure. Earlier operations are advisable.

The dismaying collapse and death of this patient following the Decholin arm-to-tongue circulation time tests would seem to indicate the possibility of a direct relationship to the Decholin which was used. A possible anophylactic or toxic reaction was considered, but investigation of this drug seems to eliminate it as a direct cause of this patient's death.

Decholin is dehydrocholic acid and is an oxidation product of cholic acid derived from natural bile acids and occurs as a fine, colorless, crystalline powder of bitter taste, slightly soluble in glacial acetic acid and alcohol. Decholin-sodium is the sodium salt of dehydrocholic acid, and is soluble in alcohol and water, forming a slightly alkaline solution used for intravenous injection.

Bile contains two characteristic salts – sodium glycocholate and sodium taurocholate. When the acids of these salts are hydrolized, they yield respectively, glycocoll and taurine, and common to both, sodium cholate. Glycocholate is found chiefly in the bile of herbivorous animals, and taurocholate in carnivorous; in human bile, there is a mixture of the two.

Decholin is a rapidly effective choleretic and cholagogue, relatively non-toxic, and in therapeutic doses, neither affects the cardiovascular, nervous, nor hematopoietic systems. When straight bile is introduced into the circulation, it has a depressant effect upon the heart muscle, leading to a reduction in blood pressure and slowing of the pulse, but intravenous injection of Decholin sodium in therapeutic dosage, which is three to ten times the dose used in measuring the arm-to-tongue circulation time, has no such effect upon the cardiovascular system, but is followed in 15 to 20 minutes by a profuse flow of bile lasting one to one and one-half hours, effecting excretion of bilirubin, cholesterol, pigment, and effects diuresis in hepatic engorgement with edema. Compared with bile constituents its toxicity is 1/10 that of sodium taurocholate, 1/13 of sodium glycocholate, and 1/22 of sodium cholate. Its only contra-indication is complete biliary obstruction.

Decholin circulation-time tests have been without undesirable side effects, so it logically follows that the collapse of this patient was due to another cause coincidental with this test, but not due to it. This patient has had many attacks of syncope related to over exertion and emotional upsets, but this was not just a fainting spell – the pulse was slow and the blood pressure elevated, at least for a time before failure of respiration and heart beat. From this, it does not appear that this catastrophe was cardiac; nor would pulmonary embolism fit this pattern for shock is inevitable. With the tonic and clonic convulsion, this is the picture of cerebral embolism.

When doubt assails me, and the next step appears more hazardous, and my convictions waver, I can get comfort from the words of Giovanni, Battista Morgagni, who in 1761 when he was eighty years of age, published his famous De Sedibus et Causis Morborum, a book which founded the science of pathological anatomy. In this Morgagni remarks, "Those who have dissected or inspected many bodies have at least learned to doubt; when others, who are ignorant of anatomy and do not take the trouble to attend to it, are in no doubt at all." So, even though I may have doubted

and would temporize and consider other possibilities before summing up, the path I have followed, though it may have been devious at times, has led me to the conclusion that this child had a congenital heart lesion which consisted of an inter-atrial septal defect or large patent foramen ovale with a superimposed rheumatic infection which resulted in atrial thrombus formation and death resulted from paradoxical embolism to the brain.

DIFFERENTIAL DIAGNOSIS

Dr. David Littman: This girl of fifteen was admitted to the hospital for fainting spells and cyanosis. At the age of five she had had rheumatic fever, which must have been severe because she was kept in the hospital for a year. It would be helpful to know exactly what occurred at that time. In any event, this patient, who should have had heart murmurs, apparently never had them. Even though she was followed by frequent intervals thereafter by any number of competent observers no murmurs were ever heard. Other details I should like to know are whether she was cyanotic at birth and the state of her mother's health during the pregnancy. In any event, at some time after beginning school at about the age of seven, she began to be cyanotic, to tire easily and to be unable to keep up with the other children — an indication that she was encroaching upon a limited cardiac reserve.

At the age of ten she began to have syncope. Syncope occurs as a manifestation of heart disease most often in Adams-Stokes disease, in complete heart block with fluctuations of rhythm, occasionally in paroxysmal arrhythmias with unusually rapid rates, in coronary-artery disease, rarely with angina, in aortic stenosis and in cor pulmonale. It especially occurs in heart disease secondary to lung disease; I can recall having several such patients whose primary complaint was fainting. I might add that no one knows why these people faint. Some of these patients also have angina pectoris or something much like angina. I have observed a man with Eisenmenger's complex who had fainting spells. In this particular case there was some question about epilepsy as well. When we saw the patient during such an attack he had ventricular tachycardia. Some patients with congenial heart disease are prone to paroxysmal arrhythmias, which in some cases is sufficient to produce syncope. It is interesting that during the terminal episode which was apparently not too unlike the previous attacks, the patient had a pulse of 70. Whether the pulse was regular or not is not mentioned. The assumption is that it was. It is interesting that she had the attacks commonly with overeffort and could produce them regularly by walking up two flights of stairs. This too is characteristic of the fainting spells that occur with cor pulmonale.

I do not know how to fit in the throbbing headaches and do not know that they contribute anything.

The physical examination was very interesting. The patient was cyanotic, and had clubbing of the fingers. I wish we had been informed whether there was any discrepancy between the degree of the cyanosis and the degree of the clubbing. The greatest obstacle in arriving at a diagnosis in this case is the absence of thrills and murmurs. There were two heart sounds or at least a split second sound, which was loud and could be felt over the pulmonary area. This suggests that the pressure in the pulmonary artery was very high. The two heart sounds in systole in the pulmonic area are troublesome. Nothing in the pulmonary valve produces first sounds; they are produced by the mitral and tricuspid valves and should be heard best over the lower part of the heart. I should have expected, with two first sounds and two second sounds, a bundle-branch block on the electrocardiogram; that was not observed, but the patient did have the pattern of hypertrophy of the right ventricle.

Dr. William R. Owen: I think everybody agreed that she had cyanosis and clubbing. In the pulmonary area I heard a systolic murmur, and a loud palpable pulmonic second sound was apparent. I estimated the murmur as only Grade 1 or 2.

Dr. Allen M. Butler: I wonder if Dr. Nadas can tell us more about these murmurs.

Dr. Alexander Nadas: I think we called the systolic murmur Grade 2 in the pulmonary area. I do not recall the other sound heard in systole. The cyanosis and clubbing were both definite; I should call them two plus or three plus.

Dr. Howard B. Sprague: Such an additional systolic sound might be related to the pulmonic and aortic valves since in opening they contribute to the first heart sound. Dr. Nadas has suggested, in valvular pulmonic stenosis,

that the accentuation of the third component of the first heart sound is due to the "slapping-sail" effect of the pulmonic valve as it attempts to open.

Dr. Littmann: May I see the x-ray films, Dr. Gibbons?

Dr. John F. Gibbons: There is a definite enlargement of the pulmonary-artery segment of the cardiac silhouette and also, in the lateral view, enlargement arteriorly of the right ventricle. The other cardiac chambers, as far as I can tell from these films, are all of normal size. The lung fields are normally vascularized. There is no abnormal indentation on the barium-filled esophagus.

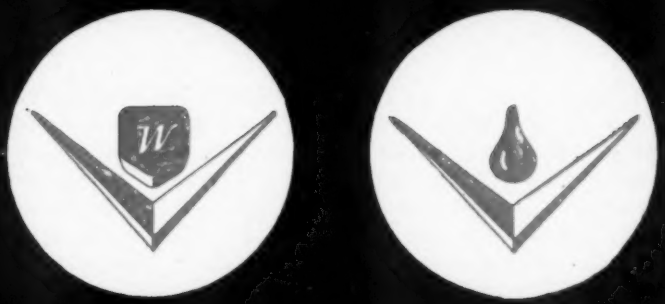
Dr. Littmann: The vascular channels in the lungs are not too large or too small?

Dr. Gibbons: If anything, they are sparse, but I think one can see good-sized vascular channels throughout the cardiac silhouette.

Dr. Littmann: Two features of the circulation times are fascinating: The amount of Decholin used, and the times themselves — seven and eight seconds. This girl, who was apparently of normal size for her age, was practically an adult. It has been my experience that in people with normal hearts an end point cannot be obtained with 1 cc. of Decholin; it takes 2.5 cc. to 3 cc. In general the amount of Decholin required to determine a circulation time varies with the speed of the circulation time. People who are in congestive heart failure and in whom a long circulation time is anticipated may require 5 cc. Only in patients with unusually rapidly circulations can one expect to obtain an end point with 1 cc. I asked Dr. Myers what the normal circulation time was for a fifteen-year-old girl. He believed that it should not be much different from an adult's — perhaps as short as twelve or as long as twenty seconds. If she had been nervous, excited or febrile, the circulation time might have gone down to eleven or ten seconds, but it surely should not have decreased to seven seconds. Was the circulation time of seven seconds, therefore, a manifestation of an abnormal shunt from right to left, or could a circulation time that brief occur in conditions with high output and rapid circulation such as cor pulmonale? I have not yet settled that question in my mind. Certainly, if there was an abnormal shunt from right to left all the Decholin did not cross the shunt into the systemic circulation. For the sake of argument, let us assume that half of it passed through the shunt. In that case I am asked to believe that an end point was obtained with 0.5 cc. of Decholin. This I find difficult to accept. It would imply that there was a defect high in the ventricular septum and that the right ventricle squirted its contents almost directly into the left ventricle.

The patient became restless and died in a fashion that is fairly characteristic of some patients with pulmonary heart disease. I have observed 2 such cases, and I have heard of others. The patient died suddenly, unexpectedly, sometimes after a meal and commonly without any apparent cause; at autopsy there was no obvious reason for death — at least there was no evidence of a cerebral or cardiac accident.

I have to decide whether this was a case of congenital heart disease, with cyanosis, or of pulmonary vascular disease or possibly a combination of the two. Most cases of congenital heart disease with cyanosis have this throughout life with the notable exception of those with Eisenmenger's complex. In this condition even though there is a shunt, or the possibility of a shunt, with an overriding aorta that receives blood from both ventricles, the amount normally entering the aorta from the right ventricle is insufficient to cause cyanosis, at least in the early years of life, but as the child grows older, vascular changes occur in the lungs. Increasing pressure in the pulmonary tree forces larger and larger quantities of blood from the right ventricle to be shunted into the systemic circuit, resulting in cyanosis. Therefore, Eisenmenger's complex is a definite possibility in a girl who manifested cyanosis at some time before her tenth birthday. Yet there are several details that militate against this diagnosis. In the first place there was little or no murmur. The few patients that I have seen — and I can number them on the fingers of one hand — all had systolic murmurs of considerable intensity and frequently diastolic murmurs, which arose from the aortic or pulmonary valve. Moreover, strain appears on both ventricles so that there is commonly no evidence of right-ventricle hypertrophy by electrocardiogram. There may be normal axis deviation and, in some cases, hypertrophy of the left ventricle. The presence of right-ventricle hypertrophy makes this diagnosis unacceptable,



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1. Martin, W. J., et al.: J.A.M.A. *160*:928 (March 17) 1956.

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at least at the moment.

Another lesion that could conceivably account for the findings is the tetralogy of Fallot in which there are sometimes few murmurs but with which there should be cyanosis from birth and evidence of inadequate physical development. This girl was well developed for her age. With isolated pulmonary stenosis there may be a large pulmonary artery, but here too I should anticipate not only a loud murmur but other manifestations. A single ventricle could conceivably have produced this picture, but I find it hard to accept. In view of the history of rheumatism, I suppose I ought to consider the possibility of mitral stenosis, which can cause cyanosis, but I am not sure it ever does to this degree. Though I have less faith in the presence or the absence of murmurs than I once had, I still find it difficult to accept mitral stenosis as occurring in a heart without any apical diastolic murmur.

The diagnosis of primary pulmonary vascular disease is one that agrees with many aspects of this case. This is a condition that, for the most part, has an unknown origin, occurs at any age, including infancy, and in either sex — in the few cases that I have looked up, it was predominantly in the female. It is thought by some to be of congenital and by a few investigators to be of rheumatic origin, but for the most part nobody quite knows the etiology of the sclerotic changes that are seen in all coats of the small and medium vessels of the pulmonary tree. In some cases there is evidence of thrombosis of the smaller vessels with subsequent organization. This I suppose is the same as Ayerza's disease or the so-called black cardiac disease. Patients with this condition show an inexorable progress with a fatal termination in a few months to as long as fifteen years. These people have weakness, vertigo, shortness of breath, cyanosis and clubbing; they may have anginal pains and fainting spells and may die suddenly. The description fits this particular case. But I wish that the circulation time had not been quite so brief. In the articles I looked up no mention was made of the circulation time except in one by Taquini et al. A few years ago they studied some 10 cases in which the circulation time was actually slow. However, all the patients were older and were in heart failure at the time. The slow circulation time may have been due in part to the heart failure and in part to the increased viscosity of the blood resulting from its high cellular and protein content.

I am left, therefore, with these two possibilities. Still another that might be considered a straddle betweeen them is primary pulmonary vascular disease existing simultaneously with a patent foramen ovale. In Eisenmenger's complex, the same situation exists; there is a congenital defect followed as in this case by pulmonary vascular disease. However, I shall say that this girl had primary vascular arteriosclerosis of the lungs and no congenital heart disease; my second possibility is Eisenmenger's complex.

Dr. Butler: Dr. Nadas was the visiting physician when this child was admitted to the Children's Service. As his period of service ended a day or two after her admission he, for the purpose of this conference, may have the advantage of not knowing the autopsy findings.

Dr. Nadas: When we talked about this patient on rounds I think I came to about the same conclusion that Dr. Littmann has reached — that is, primary pulmonary hypertension based primarily on increased pulmonary arteriolar resistance. We have seen children with identical clinical, radiologic and electrocardiographic pictures who turned out to have that condition. They also had the syndrome of weakness and syncope. I should not be surprised if one would have to straddle the fence and assume the presence of two conditions, the second being a communication between the two sides of the circulation, to explain as long lasting and as deep a cyanosis as this girl had. I should still call it primary pulmonary hypertension, however, and assume that the defect between the two sides probably did not have a casual relation to the increasing pulmonary arteriolar resistance. We have seen a series of children with ventricular defects whom we have had the opportunity of following from infancy; their lung fields always looked ischemic. They did not go through a phase of increased flow that caused pulmonary arteriolar disease and thus resulted in the picture of ischemic lung fields: if the lungs were ischemic at ten or fifteen years of age, they were also ischemic at ten months. I have seen this picture in patients whom we know have defects of the ventricular septum; hence I could bring in the diagnosis that there

was a primary pulmonary hypertension, which does not necessarily exclude the presence of a defect between the two sides of the heart, but I do not know that the two were in casual relation.

Dr. Gordon S. Myers: I might say that in this hospital we have seen patients with pulmonary vascular disease and a defect of either the auricular or the ventricular septum or a patent ductus arteriosus with little or no murmur.

Dr. H. L. Heyl: How long before death was the Decholin given?

A Physician: Actually, the patient was dead about twenty minutes after the Decholin was given, but she was not pronounced dead until forty-five minutes later; we tried for ten minutes to revive her.

A Physician: Do you think the Decholin was in any way responsible for the death?

Dr. Littmann: Literally, millions of tests are performed with Decholin, and nothing ever seems to happen. There was some warning about the use of ether in people who are assumed to have a right-to-left shunt; apparently deaths have occurred under that particular circumstance. I think in this case the use of Decholin per se had little to do with the outcome. It should be remembered that the patient had syncopal attacks with emotional trauma; perhaps the procedure itself was enough of a nervous shock to precipitate an attack.

Dr. Butler: The physicians on the service were apprehensive about carrying out procedures necessary to establish the diagnosis; they believed, however, that the diagnosis could not be made without so doing and selected as the first procedure one they assumed to be the least fraught with danger.

Dr. Littmann: Whatever the diagnosis turns out to have been this was probably not a case in which surgery would have been expected to be of benefit.

Dr. Nadas: Yes; at the same time we are justified in trying to find out all we can about a girl whose cardiac reserve was very limited and who could have had a lesion such as pulmonary stenosis and a patent foramen ovale, which, however, did not seem likely. At the time, in view of the severity of the condition, we believed that diagnostic procedures were justified.

Dr. John T. Quinby: Did you ever see a pulmonary arteriovenous shunt that was large enough to cause this amount of cyanosis but that was not visible in the x-ray films of the lung?

Dr. Littmann: To cause this amount of cyanosis I should think it would have to be visible.

CLINICAL DIAGNOSIS

Congenital cyanotic heart disease.

Pulmonary endarteritis, with pulmonary hypertension.

DR. DAVID LITTMAN'S DIAGNOSIS

Primary vascular arteriosclerosis of lungs.

? Eisenmenger's complex.

ANATOMICAL DIAGNOSIS

Congenital heart disease: aortic-pulmonary-artery septal defect. Pulmonary vascular disease.

PATHOLOGICAL DISCUSSION

Dr. Robert H. Fennel Jr.: We found at autopsy that the heart was not enlarged. It weighed 270 gm., not excessive for a patient of that size, but the right ventricle was greatly dilated and hypertrophied. The wall was 14 mm. thick, the same as the left ventricle, and in the volume of the cavity and appearance of the papillary muscles, the two ventricles were similar. The valves were all normal. Nothing suggestive of rheumatic fever was found in the valves or myocardium. The foramen ovale was closed. The origin and distribution of the coronary arteries were normal. The only abnormality of the heart or great vessels was a defect in the septum between the aorta and pulmonary artery. This was a rounded opening, 1.2 cm. in diameter, and was located 1 cm. above the upper edge of the aortic cusps. We could dissect between the aorta and pulmonary artery below the communication to make a space 1 cm. long, a distance above the right coronary artery that was probably sufficient for the surgeon to have attacked this lesion. The edge of the defect was smooth, and the walls of the two vessels seemed to be fused. Beyond the defect the aorta and pulmonary artery branched normally. There was mild atherosclerosis in the main pulmonary artery. The ductus arteriosus

"You try to scrub the bathtub with your back aching morning till night!"

"I don't know about bathtubs, but two days ago I couldn't reach a shelf higher than that."

"I thought maybe I slept in a draft. Never had a stiff neck like this before."

"That's nothing. I went around with my arm in a sling for nearly two weeks—had to sleep with a pillow at my back so I wouldn't roll over on it."

"I thought I was getting too old for high heels—low heels didn't help. My leg hurt down to the ankle."

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feet all d
but it was
my arms
bothered

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"My back was so tight I couldn't even get on and off the bus; now I can climb stairs."

"I hope he helps my knee that quick."

"Take it from me, you should be glad you saw him early in the game so he could do some good."

"Good?— why, he's got me doing exercises I haven't done in years."

the spread of common rheumatic complaints

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was closed.

Embryologically, such a defect represents incomplete partitioning of the truncus arteriosus. In the 5-mm. embryo two ridges grow into the lumen of the large vessel that extends cephalad from the heart, and these two ridges meet to separate the vessel into pulmonary artery and aorta. Presumably, in one area the two ridges did not meet in this patient, and so a communication remained. Collett and Edwards consider this a variation of a persistent truncus arteriosus and classify it as Type 5.

This is an uncommon anomaly as judged by the few available cases, only about 25 having been reported up till several years ago. That number has been increased by recent reports of cases that were diagnosed clinically either by aortography or by catheterization or were found accidentally at the time that an operation was being performed with the intent of ligating a patent ductus arteriosus. Gasul and his co-workers have diagnosed 1 case by retrograde aortography, and Dexter, at the Peter Bent Brigham Hospital, found such a case by accidentally placing a catheter through the opening between the aorta and pulmonary artery. Adams et al. also report 5 cases of this type of anomaly recognized by catheterization studies. Of the several cases that have been recognized at operation after a misdiagnosis of patent ductus arteriosus 1 is reported from this hospital and 4 cases are reported by Gibson and his associates. Gross has operated on a patient who was thought to have a patent ductus arteriosus; at operation this type of defect was found and successfully repaired. Scott and Sabiston have also performed such an operation with a successful result. It is therefore not merely of academic interest to diagnose this condition.

Most of the cases have been similar to this one. The defect is usually in the first several centimeters of the aorta, and the defect has varied from 0.5 to 3.0 cm. in diameter. There are no consistently associated anomalies, and when other anomalies are present they are usually of little significance. The clinical picture is not distinctive, and, as indicated above, most of these cases have been diagnosed as patent ductus arteriosus.

An acquired communication may simulate this condition, and some of the cases reported seem to have been of this nature. Shepherd's and Moorhead's cases are probably examples of this. There is a possibility that a patent ductus arteriosus will be mistaken for aortic-pulmonary septal defect, and Lutembacker's case seems to have been an example of such a misinterpretation.

Of the remainder of the autopsy study, only the lungs were significant. They were light and fluffy. The pulmonary arteries were conspicuous, even toward the periphery of the lung. The bronchial arteries when injected were slightly more prominent than usual, but there was no striking change in them. Microscopical study of the lungs revealed changes in the vessels that are somewhat puzzling. There was fibrous intimal thickening of the arteries and arterioles, and a few of the vessels contained organized thrombi or emboli because there were multiple lumens lined by endothelium and separated by loose connective tissue. Many of the small arteries were completely occluded by loose connective tissue. In the walls of many of these one could find multinucleated giant cells in what was apparently the lumen and adjacent to the internal elastic lamina but also farther out in the wall. In a few places evidence of phagocytosis of the elastic tissue by the giant cell was found — a picture that one sees typically in the so-called giant-cell or temporal arteritis. Also, adjacent to some of these giant cells were small flecks of calcium. There was no evidence of necrosis in the vessel wall and no evidence of an acute reaction. The media of the arteries and arterioles did not seem to be thickened.

We know from experimental observation and from what Castleman and Bland have seen in human patients that changes such as this can result from emboli. Bernard in England, injected autogenous fibrin thrombi and described acute arteritis and also described some giant-cell reaction in the walls where the fibrin was being deposited. The intimal thickening may be due to organized emboli or thrombi such as Muirhead and Montogomery produced experimentally in animals. We demonstrated no source for emboli however, and I do not know that we should particularly suspect that. Perhaps they were thrombi. The fibrous intimal thickening resembles what has been seen here in a study by Thomas and others. It is also similar in some respects to the vascular changes

that one sees in mitral stenosis.

In summary, this patient had a congenital heart lesion but had in addition pulmonary vascular changes, which I am quite sure were secondary to the congenital heart lesion, but I have no absolute proof of that. The incidence of thrombosis and embolism is so common with heart disease that I believe the associaiton is more than coincidental. Some of the intimal proliferation was undoubtedly due to the pulmonary hypertension, but I do not believe that that is the whole story.

Dr. Sprague: Was the head examined?

Dr. Fennell: It was normal.

Dr. Allan Friedlich: Are some of the changes in the pulmonary vessels similar to those described by Rich in patients with the tetralogy of Fallot? These patients also have decreased pulmonary blood flow and increased blood viscosity that may lead to thrombus formation.

Dr. Fennell: They do resemble them. I am not sure where they fit with this picture, though, because here the flow is greater, not less, than normal.

Dr. Butler: At first thought one wonders why the x-ray films did not show increased blood flow in the pulmonary vessels. I suppose, however, that pulmonary vascular disease prevents increased blood flow through the vascular bed.

Dr. Fennell: I think there must have been quite a marked embarrassment of flow through them. We injected the bronchial artery and found that the pulmonary vessels were prominent but not markedly so.

Dr. Sprague: I think the point that Dr. Nadas brought up is very important. He says that, in successive x-ray films taken over a period, he at no time saw the lungs full of blood. In the usual case in the adult, which we may see in only the fully developed state, we usually do not have the advantage of a pervious knowledge of what the lungs looked like on x-ray examination. Here, however, there is definite evidence that the pulmonary pattern was always that of decreased, rather than increased, vascularity; in other words, the vascular changes were not secondary to mechanisms of excessive blood flow.

Dr. Nadas: There is one other point. It seems inconceivable to me that a girl with a large enough left-to-right shunt to have resulted in these changes should have grown up to have a normal-sized heart at the age of fifteen. All those in whom this condition develops on the basis of a pre-existing large pulmonary flow have large hearts.

Dr. Myers: Furthermore, these changes may occur very early in life. We had a recent patient with patent foramen ovale and marked pulmonary vascular disease whose symptoms began shortly after birth and who died at two and a half years of age.

Dr. Nadas: That case was similar to the one under discussion. I have seen one at autopsy at the Floating Hospital with pulmonary vascular changes alone and no septal defect.

Dr. Fennell: I was impressed with its resemblance to the changes seen in the vessels of other patients with cogenital anomalies who have associated pulmonary hypertension.

Dr. Sprague: And they are not confined to vessels of one caliber like the ones described by Castleman and Bland?

Dr. Fennell: The most marked findings were in the small arteries. There was some thickening in the small arteries and arterioles, but the changes that I think were organized thrombi, or emboli were primarily in the small arteries.

Dr. Owen: Some believe that the Decholin was responsible for the patient's death. I wonder if Dr. Fennell knows of any such reactions.

Dr. Fennell: I am afraid I cannot explain it very well.

Dr. Myers: I do not think it is possible to be at all certain of the mechanism of death, but one possibility is that there was eventually a sharp decrease in systemic resistance, which increased the right-to-left shunt at the base of the aorta and therefore flooded the coronary and cerebral circulation with unoxygenated blood.

Dr. Edward F. Bland: The reason for this is that the systemic blood pressure had gone up.

Dr. Myers: That was the earliest effect, but the blood pressure then fell again.

Dr. Littmann: I had a patient with a different background who died recently. That was a man who had similar lung disease resulting from numerous minute emboli, essentially the Bland-Castleman condition, and who during a meal, died between mouthfuls. There was no other precipitating factor. That seems to be the usual manner of death of people with gross pulmonary hypertension.

THE *President's* PAGE

ANOTHER ELECTION IS NEAR

MANY of you have been kind in writing to me and submitting your comments on my last month's page. I wish to thank all of you for your comments and suggestions.

Another election is near. This should give us occasion to pause and reflect, as other good citizens do, on the qualifications and promises of the various candidates. Political office-holders represent us, too; and they should be reminded of that repeatedly and loudly. It shames me and grieves me to realize that the medical profession is being degraded into a maligned minority by economic planners and schemers who are intolerant of minority views and rights. I do not advocate that we must curse and rage petulantly against those who would scheme to engineer the disruption of doctor-patient relations in the guise of "better health planning"; however, we could be more virile and vocal in our arguments, and less apologetic and defensive.

Often, I have wondered, why the lay press singled out the physicians of this country as targets in a campaign of vilification? Are we really the scoundrels that have been portrayed in sensational articles? Are we being made the whipping boys in an attempt to stimulate a lagging circulation? Or do these writers honestly believe what they write, – that better medical care can be achieved through socialism and the submersion of individual rights to an all-powerful statism? Is the vilification of the doctor a maneuver in the struggle to achieve socialism? Or again, I ask, – are we really evil?

No! I cannot accept the accusation that I – or any of my colleagues are blackguards. True! – there may be some rascals in our ranks, – as in any other profession, – but truly honest efforts are made to detect, expose and punish them, or, at least, to restrain them. I am not being a Pollyanna when I say that these rascals are but a tiny fraction of our profession.

Then, why must we be defensive and apologize for wanting to do our work honestly, diligently, faithfully and exercise those skills for which we have served expensive years of training, – and ask for fair payment for these services? The plumber, carpenter, mechanic and farmer get paid. Why shouldn't we?

To convince the public that we deserve the pedestal of respect upon which we once stood, I submit that it is not necessary to engage firms of public relations experts to advertise to the world what wonderful men we are. Laudatory radio or television programs or newspaper or magazine articles are not needed. It's so simple! Let the doctor do his work with clear conscience and with the pride he deserves. Then each doctor's office will become a veritable "public relations center."

A. I. Podolsky, M.D.
President, Arizona Medical
Association

Editorial

ARIZONA MEDICINE

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The Editor sincerely solicits contributions of scientific articles for publication in ARIZONA MEDICINE. All such contributions are greatly appreciated. All will be given equal consideration.

Certain general rules must be followed, however, and the Editor therefore respectfully submits the following suggestions to authors and contributors:

1. Follow the general rules of good English, especially with regard to construction, diction, spelling, and punctuation.
2. Be guided by the general rules of medical writing as followed by the JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION.
3. Be brief, even while being thorough and complete. Avoid unnecessary words. Try to limit the article to 1500 words.
4. Read and re-read the manuscript several times to correct it, especially for spelling and punctuation.
5. Manuscripts should be typewritten, double spaced, and the original and a carbon copy submitted.
6. Articles for publication should have been read before a controversial body, e.g., a hospital staff meeting, or a county medical society meeting.
7. Exclusive Publication—Articles are accepted for publication on condition that they are contributed solely to this Journal. Ordinarily contributors will be notifed within 60 days if a manuscript is accepted for publication. Every effort will be made to return unused manuscripts.
8. Illustrations — Ordinarily publication of 2 or 3 illustrations accompanying an article will be paid for by Arizona Medicine. Any number beyond this will have to be paid for by the author.
9. Reprints — Reprints must be paid for by the author at established standard rates.

The Editor is always ready, willing, and happy to help in any way possible.

QUALITY — QUANTITY

WHEN NO less an authority than the Wall Street Journal, (15 June, 1956), tells us in headlines "Medic Merchants — Doctors Treat More Patients Faster. Some Level Fee Schedules", it is refreshing to read in a recent issue of "Look", (21 August, 1956), that one doctor finds it impossible to give good service when he is pressured into seeing 40 or more patients in one day. The "Look" piece, titled "Why I Stopped Being A Family Doctor" and subtitled "A general practitioner explains why he, like many of his colleagues, feels he can't take it any more", is good reading for us — and also for the public. The author lays it on the line. The article is brief and the reader has the feeling that it is entirely earnest. The young doctor (after all, he has been doing general practice for only three years) is tired of doing high class first aid — or "not so high class at times", he is fed up with compromising with quality, frustrated that he hasn't time to keep abreast of new medical discoveries, harassed because his personal life as a citizen and a family man is regularly sacrificed in behalf of the effort to serve all comers. He deplores the "popular myth that a doctor is a hybrid of saint and superman, indefatigable, generous, and nerveless." Young as he is, the author has obviously experienced and fully values the rewards and obligations inherent in medical service. He is no less dedicated because he forsees that in continuing bone weariness he cannot be the "good, steady, cheerful, confident doctor I want to be to all my patients".

The Wall Street Journal article, written by a staff reporter attending the A.M.A. convention in Chicago this past June, is not such good reading. A suitable sub-headline, under "Medic Merchants", might have been "Suckers Seek Subterfuges". We learn that "like many another merchandiser the 225,000 doctors who sell their services behind an M.D. license are handling a record volume of business this year". It is made clear that doctors have been slower to raise fees than other sellers of merchandise or service and that the average doctor working 62 hours per week is currently paid $4.87 per

hour. By and large, fees haven't changed in 10 years. The cost of living, according to the United States Bureau of Labor Statistics, has increased 92.8% from 1939 through 1955. In the same period general medical practitioner fees have increased only 67%, says the same bureau. A hike from $3.00 to $5.00 for a unit of medical service could provide all of that 67%!

The reporter apparently took time to interview various groups of specialists and general practitioners and selected typical answers as to methods for meeting the problem of more demand and less return. The answers fitted a pattern — work harder, work longer, work faster. Under a paragraph headline "Wasting less Time" an E.N.T. specialist was quoted, "patients' histories are taken by a secretary as soon as they come into the office. I study (sic) the histories before seeing patients in separate rooms and I have an idea of what to expect. This way I can treat four patients at a time, in different rooms, without wasting the patient's or my time." The next paragraph, headlined "More Time Per Patient" begins with a quotation from Dwight H. Murray, M.D., President of the A.M.A., identified as a general practitioner from Napa, California — "We must humanize and personalize the practice of modern medicine. We physicians should arrange our working schedules so that we can give a little more time to each patient."

It is comforting to turn from the spectacle of 2000 beat-up practitioners waiting in line for free physical exams sponsored by the American Academy of General Practice at the A.M.A. convention last June "because this is the only time some of these doctors have for a physical examination" to the quiet words of the "Look" author who refuses to see 40, 50, or 60 patients in one day and looks forward to "enough time to live, study, rest and recuperate from physical and mental exhaustion."

C.L.R.

Times have Changed
AND
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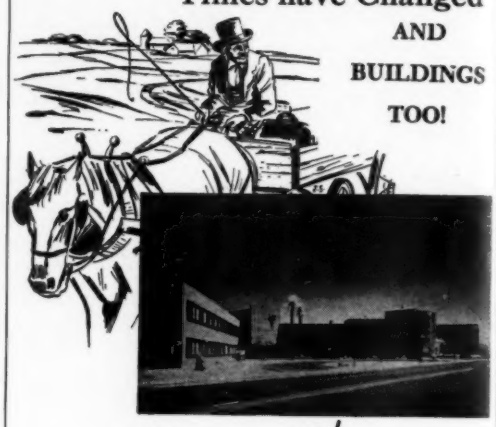
TOO!



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The History of Medicine

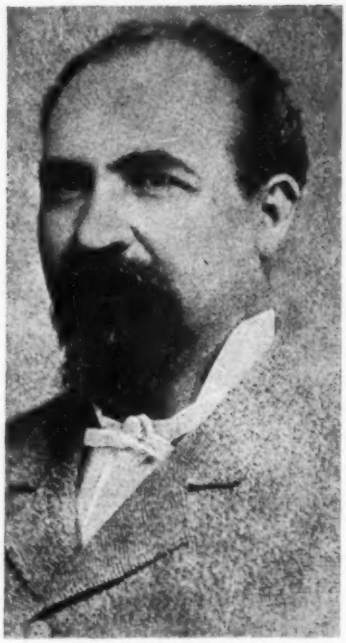
NARCISO HEREU MATAS, M.D.

(Tucson 1881-1904)

By W. V. Whitmore

THIS PROMINENT physician and distinguished citizen was born March 5, 1887, in the ancient and historic city of Gerona, in Catalina, Spain. His father was Manuel Hereu and his mother, Paula Matas, both natives of the same city and descended from old families which traced their ancestry as land owners and olive growers to the 15th century. From this union nine children were born. Dr. Matas, the eldest of the family and his hister, Theresa, were the only survivors. She is the widow of Jose Ferrer, a distinguished lawyer and author, of Gerona.

According to Spanish custom the mother's name is always appended by the offspring to the paternal patronymic or family name, and, in accordance with this usage, Dr. Matas always signed his name Narciso Hereu (the paternal name) and Matas (the maternal name) a custom which he continued in America. In consequence he was called in America by his last name, Matas, though all people of Spanish origin would have known that his family name was Hereu, omitting Matas, which was only a final tribute to his mother. He realized, but too late, that this compliment to the mother is not understood in the United States and other Anglo-Saxon countries and he should have discontinued the maternal name of Matas, or merely indicated it with a single letter M, as is done by many South Americans when they take up their residence in this country, thereby saving his paternal patronymic from confusion. Therefore, when he married Miss Theresa Jorda Ponsjoan, the daughter of a distinguished sea captain of the Port of San Feliu de Guixola (also in the province of Gerona) in 1856, their two children, Rudolph and Elvita, who were born in the United States, retained the name of Matas, while in Spain they would have been properly recognized by the name of Hereu Jorda (their paternal and maternal names). Thus it happens that Dr. N. Hereu Matas transmitted the name of Matas to his children and that his son, who has attained great distinction in this country as a surgeon, is universally known as Dr. Rudolph Matas.



Dr. Narciso Hereu Matas

Dr. Narciso (latinized Narcissus) Hereu Matas received his early and premedical education in the Catholic Seminary of Gerona, from which he was graduated Bachelor of Philosophy, equivalent to the degree of Bachelor of Arts in America.

On first coming to America with his bride in 1857, he devoted his whole attention to acquiring the English language and he made such quick progress that he was able to matriculate at the New Orleans School of Medicine a few months after his arrival, while managing a drug store which he purchased with the aid of his brother-in-law, Thomas Jorda, a resident of that city. He made such rapid headway in his medical studies that he was graduated M. D. in 1859. He then engaged in the practice of medicine at Bonnet Carre, St. John's Parish, near New Orleans, where his son Rudolph, was born in September 1860. Though only 23 years old at the time he was very popular as a physician and much esteemed in the Parish. As a result of some profitable speculations in 1861, with the outbreak of the Civil War, he decided to leave his practice and return to

Europe in order to devote himself to the study of Ophthalmology as a specialty. To this end he transferred to Paris, France, where he took special courses under deWecker and Galezowski, the greatest masters of that specialty at that time. He assiduously attended the clinics and laboratories during the two years that he studied in Paris. He then settled in Barcelona, Spain, and matriculated in the Medical School of that celebrated University where the exceptional qualifications he had obtained in Paris and in New Orleans, quickly won for him an **ad eundem** degree in medicine at Barcelona and a licentiate's diploma in the University of Madrid. He thereupon established an Eye Clinic in Barcelona and with the aid of his distinguished friends, Dr. Garreras Arago, the outstanding oculist of Catalonia, and Professor Letamendi, Dean of the profession in Barcelona, he organized a Medical Society which represented the elite of the profession in that city. He worked intensely and with great enthusiasm in his eye clinic, devoting the most of his time and thought to his professional literature and scientific interests. Unfortunately certain investments proved a disastrous venture and he was almost compelled to return to America.

He arrived in New Orleans about 1867. Here he received an invitation from wealthy members of the Spanish colony in Brownsville, Texas, and Matamoros — the Mexican city across the Rio Grande River. There with his characteristic energy and ability he soon built an extensive and lucrative practice. There his daughter, Elvita, was born. She was partly educated in Brownsville, but completed her education at the Convent of the Sacred Heart in New Orleans, where her brother was attending college and preparing for his professional career in the Medical Department of the University of Louisiana. She has never married and is now living at the old ancestral home of her maternal parents in San Feliu de Guixola, Spain. Dr. H. Hereu Matas remained on the frontier, practicing alternately in Brownsville and Matamoros until 1881, when he moved his domicile to Tucson. The following year he returned to Brownsville to aid his friends and the afflicted people of that city during the Yellow Fever epidemic that devastated the Rio Grande Valley on both sides of the river. After the extinction of the epidemic, he returned to Tucson where he resumed his practice in the fall of 1882. In 1883 he went to Hermosillo, Sonora, Mexico, where he rendered valuable assistance during the Yellow Fever epidemic that prevailed in that place.

With the exception of these two Yellow Fever relief expenditions to Brownsville and Hermosillo in 1882 and 1883, he resided continuously in Tucson until 1904, when, in failing health, he decided to visit his son, Rudolph, in New Orleans. There he had to undergo an operation for glaucoma which threatened his vision. He improved and was living at his son's home in happy and affectionate surroundings, when he was suddenly stricken by apoplexy and died in his son's arms on April 13, 1904. He died about one month after he had attained his 67th birthday. His remains are interred in his son's family tomb at Metairie Cemetery in New Orleans.

He is survived by his only remaining sister, Theresa Hereu de Ferrer who resides in Torroella, Province of Gerona, Spain, who is still active at the age of 95 years. His daughter, Elvita, who has resided in Spain since her mother's death, and his son Dr. Rudolph Matas, who is now an Emeritus Professor of Surgery at Tulane University and one of the most distinguished and honored surgeons of the South.

In 1893 he married Mrs. Louisa M. Mallet who was born in Brownsville, Texas, of French and German ancestry, and from this union a daughter, Irene, was born, who since her mother's death resides in Los Angeles, Calif.

Dr. Matas was an enlightened, progressive and unusually well educated physician who loved his calling and kept himself informed in everything pertaining to his chosen profession. He was familiar with English, French and Spanish literature, speaking these languages fluently. He was naturally of a literary turn of mind and the thorough academic training that he had received in the Seminary of Gerona had given him a perfect mastery of his native Spanish, which he wrote and spoke with the force and elegance of a classical scholar. Despite his constant occupations and preoccupations, he found time to indulge in poetry and in essays which revealed his literary tastes and culture.

Withal, he was an ardent admirer of the English language and literature and his affection for American people was boundless. The

United States was the country of his adoption and he was ever loyal to its ideals, though true to his love for the mother country.

In 1892 he was a member of the International Medical Health Association which met in Mexico City and was a member of the first Mexican Medical Congress held in that city, taking an active part in its work, especially in the Surgical and Pathological Sections.

During his residence in Tucson he served as County Physician and as City Health Officer – also had been medical examiner for nearly all of the fraternal societies and life insurance companies represented in Tucson, and was pension examiner, one term. As a side issue he was interested in gold, silver and lead mining and in several of his mining ventures was quite successful. He took great interest in civic affairs. He was a director of the Tucson Street Railway, of which he was one of the organizers and was president for a time. In this and other ways he contributed to the development of the city.

In politics, Dr. Matas was independent. In religion, though a hereditary Catholic, he was a free thinker, unprejudiced and liberal toward all religious creeds. In his social relations he was a Mason, a member of the Benevolent Protective Order of Elks and of the Ancient Order of United Workmen. In medicine he was thoroughly honorable, ethical and free from shame. He was a member of the Arizona Medical Association and a firm believer in medical organization. Quite apart from the early papers that he contributed to medical literature, while a specialist on the eye, in Barcelona, he wrote a number of very able articles and essays upon subjects and notably on Yellow Fever in which he had much experience. As a thoroughly cultured and conscientious student, a fine observer, of broad vision and unquenching thirst for knowledge – which he displayed up to the last moments of his life – his counsel was of exceptional value as a clinician at the bedside, and won for him a place in the foremost ranks of his profession.

PUBLIC RELATIONS AWARD — Blue Cross — Blue Shield

Pictured are Dr. G. Robert Barfoot, 2037 N. Central, Robert R. Rinehart, 6003 E. Cheney,

Left to Right: Dr. G. R. Barfoot, Phoenix; Robert R. Rinehart, Scottsdale; Dr. C. B. Warrenburg, Phoenix.

Scottsdale, and Dr. Clarence B. Warrenburg, 5835 N. 2nd Ave. The three are admiring the trophy presented the Arizona Blue Cross-Blue Shield by the Blue Cross-Blue Shield Commissions for its wining the overall public relations competition for plans under 200,000 in Canada and the United States.

The award marks the seventh first place award for the Arizona Plan in the past six years, the twelth presentation honored by Rinehart since the awards were originated in 1946 when he was associated with the Columbus, Ohio Blue Cross Plan. The presentation was made this year at the national Blue Cross-Blue Shield public relations institute which was held at the University of Wisconsin, Madison. John McGehee, executive secretary of Kiwanis International was chairman of the judging committee.

The winning entry dealt with newspaper, billboard and radio advertising, subscriber relations, hospital relations, medical relations and employee relations.

Dr. Barfoot is president of Blue Shield. Dr. Warrenburg is vice president of Blue Cross, while Rinehart is public relations director for both prepayment plans.

TOPICS OF *Current Medical* INTEREST

RX., DX., AND DRS.

By Guillermo Osler, M.D.

POLIO VACCINE got off to such a bad start that it is hard to believe the progress in 12 to 18 months. . . . The vaccine is now said to be 100% safe. It is very effective in preventing paralytic cases. It is most effective when all three injections have been given. . . . The public has not kept up with the good news, and it is hard to blame them. Even in Chicago, with a serious epidemic, free vaccinations were met with apathy. . . . Not so bad as in some Oriental countries, where propaganda says that white doctors eat children. It takes more selling to put a drug or procedure across in such circumstances.

In the dim distant past (30 years ago!) it would have been a sensation to hear of the SYNTHESIS OF A MAJOR HORMONE. Now it is a paragraph. . . . du Vigneaud and associates at Cornell have put together VASOPRESSIN, a pituitary hormone formerly extracted in tiny amounts from the gland of hogs. . . . The substance is non-allergenic, and equal in strength to the natural extract in cases of diabetes insipidus.

Cooking PORK has been strongly recommended to prevent transmission of trichinosis. . . . It is now probable (tho not certain) that TOXOPLASMOSIS is also transmitted by uncooked pork. . . . The disease is now very common, tho very mild, and 30 to 70% of middle-age adults are infected in certain areas. . . . There may be some other unknown means of transmitting the disease to man. The disease resembles a pneumonitis.

Dr. Maria Schnee Haynes has a set of basic rules on how to be HAPPY THO SLIGHTLY DECREPIT. Dr. Haynes is a Ph.D. at UCLA, and came from Austria. . . . Her rules suggest that one must start at an early age. (Perhaps this is what our children could be doing instead of patronizing us.) 1. Find out, when you are young, what qualities in old people are admired by the young. Remember them. 2. Never praise the good old days. Live in the present. 3. Learn to be well-balanced and to control anger. 4. Keep alive intellectually. This means not only cultural activities, books, but an interest in all things about you. (Whoops! maybe it includes baseball, T.V., etc.?) 5. Maintain perfect personal hygiene. 6. Start to be pleasant when young. You can't suddenly be a pleasant old man.

'GERIATRICS' journal, 'devoted to Diseases and Processes of Aging', uses the summary-at-the-beginning-of-each-article technic. . . . The July issue had a good discussion of PERIPHERAL VEIN problems. You must take a calculated risk if you use a conservative program for varicose veins. Thrombosis and inflammation of leg veins may be handled by drug and surgical therapy. . . . If it is the ARTERIES which are in trouble, by-pass operations are very helpful for occlusion of the iliac and femoral vessels. Arterial homografts are best, and 92% of 73 cases at Baylor (de Bakey, et al.) had a good symptomatic result.

Schering has put out an amusing, king-size folder to describe their 'Sigmagen'. It is another shotgun drug which contains a STEROID drug (prednisone), ASPIRIN, an ANTACID, and VITAMIN C. . . . The folder shows a candid-camera view of 13 people and a dog, sitting on a bench, and almost all but the dog were griping about their aches and pains or giving testimonials to their relief. . . . It is notable that the advertising states that the drug should not be used in patients with peptic ulcer, agitated psychotic states, acute exanthems, herpes of the eye, and TUBERCULOSIS. . . . This leaves the small problem of diagnosis up to the physician. A few well-placed questions would help, but so would an x-ray of the chest.

NYLON has some interesting qualities, and some unusual usages. It would not be easy these days to say which hospital furnishing was made of nylon because it was flexible, light in weight, would withstand boiling and many chemicals, was not noisy nor chilly. . . . Hospital Topics' reports that this item is a nylon bedpan.

Scotland was one of the first countries to report on the use of PAS (para-aminosalicylic acid) as a treatment for TB. . . . They should know what they are talking about when they say that PAS has an ANTI-THYROID ACTION, and may produce hypothyroidism and sometimes a goiter. . . . We don't see it in this country, but maybe we should look more intently. . . . Macgregor and Sommer even suggest that all patients who receive PAS for more than 6 months should be given small doses of thyroid extract.

It is hard to decide what a trade-journal for drug stores resembles most. The 'West Coast Druggist' is a combination of high-pressure advertising for drugs and toilet articles; homage to drug houses, drug discoveries, and top salesmen; notices of new dealerships; summaries of legal rulings; discription of display methods; book reviews; gift suggestions; contest offers; product descriptions; sales talk; etc. . . . Quite a lot like,

HOSPITAL BENEFIT ASSURANCE
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BRANCH OFFICE: 507 VALLEY NATIONAL BUILDING TUCSON, ARIZONA · 3-9421

MEDICAL DIRECTOR
DUKE R. GASKINS, M. D.

Dear Doctor:

As of July 31, 1956 some 110,000,000 persons in the U. S. . . . an all time high . . . were covered by hospital insurance. In addition, 94,000,000 people had surgical protection.

This, Doctor, means that you probably are going to have to become accustomed to filling out more forms when your patients are hospitalized.

We, here at HBA, are very proud of the fact that we make the paper work for the doctors the least possible. In most cases, 97 per cent of them, the doctor only needs to fill out a short surgical bill form so we'll know the amount to pay. Previously, we tried asking only the doctor's statement, but so often they said only "Balance Due" that we had to use the present bill form.

On 2 or 3 per cent of the cases hospitalized, it is necessary that we have additional information to make a just decision. In those cases, we appreciate your help and cooperation. If, at any time, you have any questions please be sure and get in touch with me.

Very truly yours,

HOSPITAL BENEFIT ASSURANCE

Duke R. Gaskins, M.D.
Medical Director

DRG:sk

to be sure, a modern drugstore.

To prevent someone surprising you with the fact that United Solvents Inc. is about to open a plant which turns out 1,500,000 pounds per year of REACTOR-GRADE ZIRCONIUM SPONGE, we can say that it is used as a structural material for atomic reactors, and that the Atomic Energy Commission is buying two-thirds of the output from U.S.I. . . . It 'clads' uranium, since it has a low nuclear cross-section, and lets neutrons pass thru. It also has a high corrosion and heat resistance. . . . Another element, hafnium, which is always associated with zirconium in nature, must be removed. . . . This data will not allow you to converse freely with a physicist, but it may impress a few people at the next large dinner party.

In spite of all the hospital journals and all the hospital meetings it is not easy to find clues to successful hospital administration. 'The Modern Hospital' has analyzed the evidence as to what makes an INEFFICIENT ADMINISTRATOR inefficient. It may be due to his/her having, — 1. An all-or-nothing complex, or "perfect solutions only; no compromise". . . . 2. An urge to act from expediency. . . . 3. An obsession to win, even if only a moral victory. . . . 4. A tendency to classify everything as black or white. . . . 5. No sense of proportion or balance (the mountain-out-of-a-molehill urge).

Who says the Guvment doesn't TRUST doctors? It would seem as if Congress does, after the way they lowered the social security age for disabled workers, and put the decision as to disability in medical hands. . . . The age was lowered to 50 (vs. 65), and the impairment is to be 'physical or mental which will result in death, or be prolonged and indefinite'. . . . It could include 250,000 persons.

ANTIBIOTIC NEWS, — Garrod of London reports a remarkable efficacy of Terramycin in treating PERITONITIS from a perforated viscus. . . . Anwar and Turner urge, on the basis of experimental work, that Terramycin or penicillin be used in addition to tetanus antitoxin in cases of clinical TETANUS. The drugs are effective against Cl. tetani. . . . The current dose of VIOMYCIN in tuberculosis therapy is 2 gm twice weekly. It should be used with PAS or isoniazid, and in cases which are intolerant or resistant to other agents. . . . Oral tetracycline is quite effective in cases of ACNE, in spite of the insensitivity of isolated bacteria. . . . Lich insists that "there is nothing to be gained" by starting chemotherapy in chronic urinary tract infections before specimens are obtained for SENSITIVITY TESTS. . . . Terramycin ophthalmic solution is now shown to be far less irritating and probably more effective in preventing OPHTHALMIA NEONATORUM than silver nitrate.

HORMONE ITEMS.—HYDROCORTISONE 'vaginal tablets' will give prompt relief of itching from any infectional origin. There is a time lag after fungicidal agents are started before the pruritis subsides, and the steroid stuff fills the gap. . . . PROGESTERONE has been found to increase the remission rate of postpartum psychosis to nearly 100% in a series of Bower and Altschule. . . . Hydrocortisone SNUFF produced 'complete control of symptoms' in 23 of 24 patients with hay fever who had not responded to previous therapy, including antihistamines to the limit of tolerance. . . . LUPUS ERYTHEMATOSUS can be brought under control by prednisone or prednisolone, but Dubois recommends a routine use of an 'ulcer regimen', plus a low sodium diet.

NOTICE

Meeting of the Arizona Pediatric Society in Tucson the evening of November 16th and at 10:00 a.m. November 17th.

Speakers: Dr. Otis Miller — Periatric Dermatology. Dr. Butcher — Congenital Heart Disease.

St. Mary's Hospital, 8th Floor.

All doctors cordially invited to the Scientific Program.

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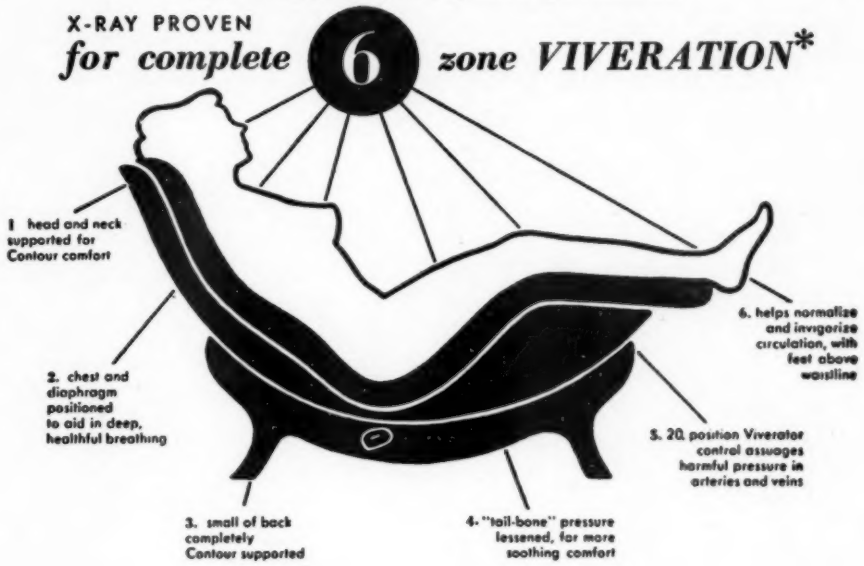
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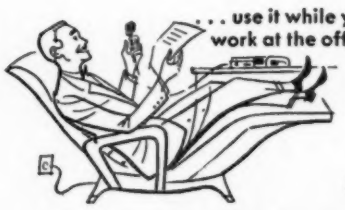

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ATARAXOID is a unique, new combination of STERANE and ATARAX, which now permits simultaneous symptomatic control and reduction of attendant anxiety and apprehension in rheumatoid arthritis and other indications.

The added tranquilizer control, desirably easing mental stress, also directly assists clinical progress. It minimizes the chance of exacerbation related to emotional strain and facilitates patient confidence and cooperation in the therapeutic program toward maximum rehabilitation.

ATARAXOID exerts the anti-rheumatic, anti-inflammatory activity of STERANE distinctly superior to previous steroids, effective in radically reduced dosage, and with minimal disturbance of electrolyte and fluid metabolism.

The ataractic effect is a central neuro-relaxing action – the result of a marked cerebral specificity – free of mental fogging and devoid of any major complications: no liver, blood or brain damage. This peace-of-mind component is also used in the lowest dosage range.

Supplied: Each green, scored, ATARAXOID oral tablet contains 5 mg. prednisolone (STERANE) and 10 mg. hydroxyzine hydrochloride (ATARAX). Bottles of 30 and 100.

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simultaneously controls the symptoms and the apprehension

In Rheumatoid Arthritis, other collagen diseases, bronchial asthma and inflammatory dermatoses

*Trademark

Organization PAGE

Norman A. Ross, M.D.

AMERICAN CANCER SOCIETY, ARIZONA DIVISION, 1459 North 1st Street, Phoenix, Arizona.

The American Cancer Society, Arizona Division is anxious to make available to the physicians of Arizona pamphlets and educational leaflets that can be used by their patients and possibly distributed in the doctors' offices. For example a booklet entitled "Care of your Colostomy" has been prepared and is available for the use of patients having had this operation. It is a supplement to medical instruction and therefore, its distribution should be through physicians.

Another new publication entitled "Give your Doctor a Chance" is an attractive 25 page pamphlet designed to answer fully and reassuringly, lay questions about cancer detection and examinations.

GIVE YOUR DOCTOR A CHANCE is a comprehensive, graphically illustrated explanation of the nature of cancer — with emphasis on the facts about metastasis as the reason for the need of early diagnosis and treatment.

AMERICAN CANCER SOCIETY, News Service, 521 West 57th Street, New York 19, N.Y.

The resignation of Dr. Charles S. Cameron as medical and scientific director and vice-president of the American Cancer Society, effective after November 1 is announced.

Dr. Cameron will become dean of Hahnemann Medical College, Philadelphia, the institution from which he received his medical degree in 1935.

Dr. Cameron joined the Society in 1946, serving as assistant medical and scientific director and professional services director before becoming medical and scientific director and vice president in 1948.

Dr. Cameron's successor will be named by the Board of Directors at a later date.

• • • •

The Editor forwarded to this office our Blue Shield letter under date of August 23, 1956, from the President of Arizona Blue Shield. We had also placed the letter in our file for this page.

Dr. Barfoot is to be commended for this explanatory letter to participating physicians. The questions and answers as relate to the activity of Arizona Blue Cross and Blue Shield nationally, including identification of Medical Indemnity of America, Inc., are things we need to know.

We suggest additional questions that could be answered and with explanation.

We are told who owns Medical Indemnity of America, Inc. Who owns Arizona Blue Shield?

We have a physicians' fee schedule established in the Service Groups in the Arizona Plan. Who is empowered to reset the fee schedule in the local non-profit Arizona Blue Shield Plan? Who sets the fee schedule in the national stock company, the Medical Indemnity of America, Inc.?

How many financial reserves be expended by Arizona Blue Shield? How by Medical Indemnity of America, Inc.?

• • • •

THE SALVATION ARMY, 631 North 7th Ave., Phoenix, Arizona.

Excerpts from a brief address by Herbert Hoover at the Annual Luncheon Meeting of the Salvation Army in San Francisco, June 22, 1956:

"No one needs explain The Salvation Army. No one needs describe its multitude of good work. The main thing to do is to give them more money to do more good works. In addition to our money, we can give encouragement to all its members for their devotion; we can express our gratitude to them and our confidence in them."

• • •

"No matter what Utopian Government men may dream of, Governments live on statistics, and averages, and politics. They do not reach into the human heart. Governments cannot regenerate character or faith or courage which restores the dignity of individual men and women."

"• • • We must always have The Salvation Army at our side."

• • • •

Secretary's Letter, AMERICAN MEDICAL ASSOCIATION, 535 North Dearborn Street, Chicago 10, Illinois.

DEDUCTIONS FOR REFRESHER COURSES

The U. S. Internal Revenue Service has just

issued a regulation which is important to physicians.

Efforts over a long period of time by the A.M.A. Law Department to get the Internal Revenue Service to issue a regulation permitting physicians to deduct their expenditures in taking post-graduate "refresher" courses have finally paid off.

The regulation, effective on August 9, provides that expenditures for education are deductible if they are for a "refresher" or similar type of course taken to maintain the skills directly and immediately required by the physician in his employment or business. An educational course to be covered should be designed for established medical practioners to help them keep abreast of current developments in the profession; it should be of short duration; it should not be taken on a continuing basis, and should not carry academic credit. Education designed to prepare the practitioner to enter a specialty will not be acceptable.

When a physician travels away from home primarily to obtain "refresher" education, his expenditures for travel, meals, and lodging while away from home are deductible. However, expenses for personal activities such as sightseeing, social visiting or entertaining, or other recreation will NOT be allowed.

• • • •

The proposal, A Medical School for Arizona Within Five Years, has received several boosts, not the least of which are these facts: New Mexico will start its two-year medical school in 1958, and their request for appropriations for operation of same, believe it or not, is $150,000 per annum.

This statement of cost, the confidence elective officials and our public has in our teaching interest and ability, explains the work of such men as Senator Harold C. Giss of Yuma County and his fellow legislators on the Legislative Council. They propose that a program or study committee be developed in preparation for a medical school. The Legislative Council is moving ahead on this project and the Arizona Medical Association has been advised that the Council looks to our association for participating and for guidance.

• • • •

THE NATIONAL FOUNDATION FOR INFANTILE PARALYSIS, 120 Broadway, New York, N.Y.

The National Foundation for Infantile Paralysis announces that postdoctoral fellowships are available for full time study in preparation for careers in research and/or academic medicine, or in the clinical fields of psychiatry; rehabilitation; orthopedics; the management of poliomyelitis and preventive medicine.

Your applications may be submitted for these fellowships at any time. The meetings of the reviewing committee carry the dates of September 1, 1956; December 1, 1956; and March 1, 1957.

Address Miss Edith A. Aynes, Coordinator of Information, Division of Professional Education of the National Foundation for particulars.

You may look for additional notices on this page.

• • • •

BOYS' CLUBS OF AMERICA, Inc., 381 Fourth Avenue, New York 16, N. Y.

BOYS' CLUBS OF AMERICA RECEIVE CONGRESSIONAL CHARTER

The First Congressional Charter granted to a national boys' organization in forty years is announced in the Boys' Clubs Bulletin. Similar bills introduced in the United States Senate and House of Representatives, co-sponsored by Senator Everett M. Dirksen and Senator Clinton P. Anderson and Representative Emmanuel Celler were passed unanimously, President Eisenhower signing the same into law.

• • • •

THE CRIPPLED CHILDREN'S DIVISION Program, State of Arizona, Department of Public Welfare. This pamphlet is available from the Department of Public Welfare and is suggested as an excellent one for the doctor's waiting room.

• • • •

MEETINGS:

A.M.A.'s Council on Industrial Health, February 3-6, 1957, Biltmore Hotel, Los Angeles, California.

The University of Texas, M. D. Anderson Hospital and Tumor Institute, Houston, Texas, November 9-10, 1956.

1957 ANNUAL MEETING

THE 66th Annual Meeting of our Association is scheduled to meet in Yuma, Arizona, April 10 through 13, 1957, with headquarters at Stardust Hotel. It is not too early to start planning for this important event and your Scientific Assembly Committee under the program chairmanship of Doctor Carlos C. Craig, President-Elect, has been hard at work developing an outstanding scientific presentation. This is the first of a series of articles which will introduce to the membership the guest orators who have accepted our invitation to participate, together with other items of interest.

Introducing Henry Dean Brainerd, M.D., of San Francisco, California.

Doctor Brainerd was born December 3, 1914. He received his A.B. degree at the University of California in May, 1935, and his Doctor of Medicine degree at the University of California School of Medicine in May, 1939. Interned at San Francisco Hospital during 1938-39; Assistant Resident in Medicine at University of California Hospital 1939-40; Resident Physician in Communicable Diseases at Boston City Hospital and part time Instructor in Communicable Diseases, Faulkner Hospital School of Nursing, Jamaica Plains, Massachusetts during 1940-41; Resident Physician in Medicine at University of California Hospital 1941-42; Clinical Instructor in Medicine and Pediatrics at University of California School of Medicine and Clinical Instructor in Pediatrics at Stanford University School of Medicine during 1942-47; Assistant Clinical Professor of Medicine and Pediatrics (University of California) and Assistant Clinical Professor of Pediatrics (Stanford) 1947-51; William Watt Kerr Associate Professor of Clinical Medicine 1951-55 and Professor of Clinical Medicine (both at the University of California School of Medicine) 1955 to the present time. During 1942-51 he was also Physician in Charge of Isolation Division, Department of Public Health, San Francisco Hospital; 1948-56 Consultant in Infectious Diseases and Internal Medicine at University of California, Student Health Service; 1951-56 Chief of Medical Service at San Francisco Hospital; and August, 1956 to date, Chairman, Department of Medicine, University of California School of Medicine, and Physician-in-Chief, University of California Hospitals.

Henry D. Brainerd, M.D.

Doctor Brainerd is the author of numerous articles in the field of infectious diseases and chemotherapy.

The House of Delegates will meet Thursday and Saturday mornings, April 11 and 13, 1957, respectively (Stardust).

Council will hold its annual meeting Wednesday morning, April 10, 1957 (Stardust).

The Annual Corporation Meeting of Arizona Blue Shield is scheduled to meet Wednesday afternoon, April 10, 1957 (Stardust).

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SUED FOR SLANDER!

Before releasing the results of an employee's examination, be sure to get his permission in writing.

When an employer underwrites the cost of a pre-employment or periodic physical examination of an employee, he generally assumes that the findings of the examination will be submitted to him direct and that the employee's permission to do this need not be obtained beforehand.

This poses an ethical and legal problem sometimes overlooked by the examining physician.

By reporting to an employer the physical condition of an employee, without first securing the employee's approval, does the doctor violate either the patient's trust or the civil law of his State relating to confidential communications? In most cases the answer is that he violates both, as a result of which he therefore lays himself open to possible suit for slander.

Some medical men who do physical examinations may reason that when a worker submits to a checkup at the request of his employer, either to hold a job or to get one, he fully understands the purpose of the procedure. They conclude that in accepting this requirement of the employing organization, the employee gives tacit permission to the physician to submit direct to that organization the findings of his examination.

But is this a safe assumption? In event of litigation, will a court recognize such implied permission?

It may; or it may not. In any case, it is obviously wiser for the physician to protect himself fully by actually obtaining the patient's consent in writing.

The following waiver form, used or modified to suit individual needs and used routinely in mimeographed form, is hereby submitted:

"The undersigned grants permission and requests Dr.....to convey full information to.....(employer) about the results of a physical examination of the undersigned on.....(date), and waives on behalf of himself and any other person who may have an interest in the matter all provisions of law relating to the disclosure to .....(employer) of information acquired thru the aforesaid examination."

Signature of person examined.....
Date. Witness .....

Such a form, properly executed and signed by the employee, constitutes comfortable and tangible assurance for the examining physician that he will not be the unfortunate recipient of a court judgment at some future date.

Admittedly, the risk of a suit for slander is not great. Yet it is always a possibility. So why take a chance?

J. D. Hamer, M.D., Chairman
Medico-Legal Committee

SOCIAL SECURITY — R.H. 7225

The President of the United States signed into law the Social Security Amendments of 1956 (H.R. 7225) on August 1. The amended law now lowers the retirement age of women as specified from 65 to 62, and authorizes cash disability benefits for workers from age 50 upwards, if they become permanently and totally disabled. The Senate, even tho its Finance Committee after prolonged study and hearings did not report the bill out favorably, passed it, with these amendments, just before adjournment, by a narrow vote of 47 to 45. The Republican Senator from Arizona voted against the law with its amendments, while the Democratic Senator voted aye.

As amended by the Senate, and concurred in by a conference committee with the House, the Law sets up a Disability Insurance Trust Fund as an entity separate from the Old-age and Survivors Insurance Trust Fund. Beginning Jan. 1, 1957, it increases Social Security taxes by ¼ percent each on employers and employees, and ⅜ percent on the self-employed, wherein the law as originally written would have increased the taxable rate at ½ percent more on each contributor. This law also extends Social Security coverage to about 600,000 additional farm owners and operators, and about 225,000 self-employed lawyers, dentists, and others. So far, doctors of medicine are excluded. The aggregate tax increase next year is expected to yield approximately $850,000,000.

Until or unless new regulations are issued, doctors will follow the same procedure in connection with this new Law that they followed under the disability freeze amendments now in effect, and passed in 1954. The physician will make his medical findings on a prescribed form, and turn in his report to the State Agency in

charge, usually the Office or Department of Rehabilitation or Social Security as designated in each district. The decision as to disability of any applicant is then made by the Agency, based on the vocational and medical findings, as to the applicant's disability, and benefits.

We physicians wonder now. Is this it? What is next on the agenda? Are we to be lassoed next? One wouldn't be surprised, whether the majority desired this type of compulsory taxation or not. We have felt for a long time, and have lifted up our voices en mass in Washington along with many other socialistic fearing souls, that there is grave danger in the enactment of these Sections of the Social Security Act; an act authorizing the Federal Government to initiate a cash disability insurance program. Restricted, of course, for a starter, but the first of other all-encompassing measures that are on the agenda in future Congressional Sessions which will eventually lead directly and rather quickly to the complete nationalization or socialization of medical practice.

Obviously, with the dozens of witnesses appearing before the Senate Finance Committee in open hearings on this Bill last spring, representing many professions, businesses, and others representing large segments of our population, have continued to fail in their endeavor to discover methods to make their opinions and wishes felt before Congress in this Democracy of ours. Loud and extended protests on the part of some segments of the populace have failed again. Thousands of wires and letters must have reached Washington and the White House urging defeat or veto of these amendments.

Why did the President sign this Bill into Law? No simple analysis can set forth all the forces which played a part in his willingness to endorse this Social Security bill, sponsored by the Democrats. This, in spite of the fact that two of his own Cabinet members, Secretaries Hobby, and more recently, Mr. Folsom had testified against adoption of H.R. 7225. From a review of the statements made in connection with signing this Bill, one gathers very plainly that he signed it because he was wholeheartedly in favor of its provisions, and what it was designed to accomplish.

The medical profession, among others, are now caught in a skillfully managed social revolution. After defeat of the National Compulsory Health Insurance Acts of 1945, and again in 1947-48, tactics had to be changed in 1950. The piecemeal approach to the same end-result was adopted, so that Congress enacted in 1950, 1952, 1954, bills and amendments, to the preceding Laws, which paved the way for the Disability Insurance set-up. And the President has signed H.R. 7225 into Law.

One wonders whether this is now the time to succumb completely to despair? You doctors had better sharpen your pencils, and begin practicing up a bit on your penmanship, so all the Federal employees can read your writing. Better begin to look around for a Union to join, then get your Social Security Card, and take your place on the payroll of a Socialistic Dictatorship. Time's a-wasting, and it may be sooner than you think.

J. D. Hamer, Chairman
Committee on Legislation

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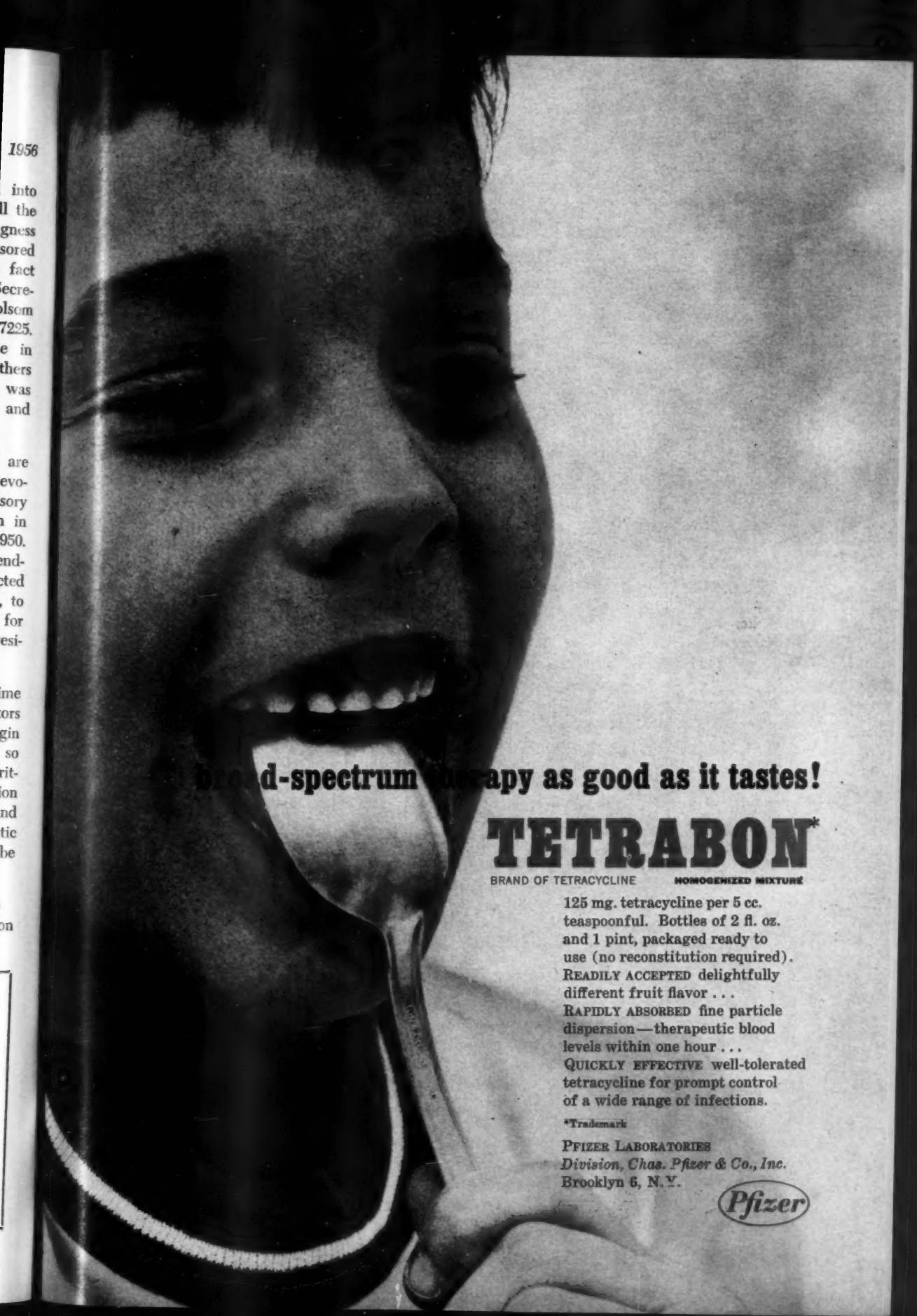
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READILY ACCEPTED delightfully different fruit flavor . . .
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QUICKLY EFFECTIVE well-tolerated tetracycline for prompt control of a wide range of infections.
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Notes From Desk Of The Executive Secretary

U. S. INTERNAL REVENUE — REGULATION POSTGRADUATE "REFRESHER" COURSES

EXPENDITURES DEDUCTIBLE

The U. S. Internal Revenue Service has issued a regulation which is important to physicians.

Efforts over a long period of time by the A.M.A. Law Department to get the Internal Revenue Service to issue a regulation permitting physicians to deduct their expenditures in taking postgraduate "refresher" courses have finally paid off.

The regulation, effective on August 9, provides that expenditures for education are deductible if they are for a "refresher" or similar type of course taken to maintain the skills directly and immediately required by the physician in his employment or business. An educational course to be covered should be designed for established medical practitioners to help them keep abreast of current developments in the profession; it should be of short duration; it should not be taken on a continuing basis, and should not carry academic credit. Education designed to prepare the practitioner to enter a specialty will not be acceptable.

When a physician travels away from home primarily to obtain "refresher" education, his expenditures for travel, meals, and lodging while away from home are deductible. However, expenses for personal activities such as sightseeing, social visiting or entertaining or other recreation will NOT be allowed.

The Social Security bill (H.R. 7225) now is the law of the land — Public Law 880 of the second session, 84th Congress. We are printing in full the statement issued by the President when he signed the bill, so you will know his position and his reasons for taking the action. Increased OASI taxes to support payments to the disabled at age 50 become payable on January 1, 1957. Disability benefits become payable on July 1, 1957. Until and unless new regulations are issued, doctors will follow the same procedure in connection with this new law that they follow under the disability freeze amendment now in effect. The physician makes his medical findings and turns in his report to the state agency in charge, usually the office or department of rehabilitation. The decision then is made by the agency, based on vocational as well as medical findings, as to the applicant's disability.

Following is the complete text of a statement issued by President Eisenhower August 1 when he announced he had signed the social security bill, H.R. 7225:

"I have today signed H.R. 7225, the Social Security Amendments of 1956. The new law embraces a wide range of changes in old-age and survivors' insurance, the public assistance programs, and child welfare services.

"This Administration's strong support of the social security program was demonstrated by the broad expansion and improvements enacted in 1954 at my recommendation. The 1954 Amendments, which extended coverage of the program to millions of additional persons and included higher benefits for all who were then or who would become beneficiaries, have had a major impact in bringing greater security to our people.

"The new law also contains certain major provisions which were recommended by the Administration. It extends social security coverage to about 600,000 additional farm owners or operators and about 225,000 self-employed lawyers, dentists, and others.

"It provides for increased Federal funds to encourage better medical care for the needy aged, blind, disabled, and dependent children. This will help meet a critical problem for these groups.

"Another Administration proposal placed increased emphasis, in public assistance programs, on services to help more needy people build toward independence. The law initiates new programs of grants to train more skilled social workers and to support research in ways of helping people overcome dependency. Another Administration proposal will increase funds for child welfare services.

"The law also includes provisions about which the Administration had serious reservations in their initial form; these provisions were modified and improved before their final enactment and now meet, in part, some of the Administration's objections.

"The original proposal to lower the retire-

ment age for all women was changed to provide that employed women and wives may accept reduced benefits at an earlier age or obtain full benefits at age 65. I am hopeful that this provision will now have no adverse affect on employment opportunities for older women. The law allows full benefits at age 62 for widows because of their special needs.

"Congress also modified somewhat the original proposal to provide disability benefits at age 50 or above. A separate trust fund was established for the disability program in an effort to minimize the effects of the special problems in this field on the other parts of the program — retirement and survivors' protection. We will, of course, endeavor to administer the disability provisions efficiently and effectively, in cooperation with the States. I also pledge increasing emphasis on efforts to help rehabilitate the disabled so that they may return to useful employment.

"The original proposal would have imposed a 25 percent increase in social security taxes on everyone covered by the system. I am pleased that the tax increase has now been cut in half. Our actuaries report that while they cannot estimate costs of the disability program with certainty, the tax increase should be adequate to finance the benefits, assuming effective administration.

"Although there were differences of opinion over separate provisions, the final legislation was approved overwhelmingly by Congress. In signing this legislation, I am hopeful that this new law, on the whole, will advance the economic security of the American people."

THE RECORD

The Congressional Record of July 18, 1955, page 9304, shows that Representative Rhodes VOTED FOR passage of H.R. 7225, and that Representative Udall did not vote but was paired with Mr. Crumpacher of Indiana. This was a "general pair," therefore it is not possible to ascertain whether or not Mr. Udall favored passage. In any event, none of our Representatives positively opposed passage of this bill. You will recall the House of Representatives by a roll call vote of 372 to 31 under a procedure (suspension of rules) barring amendments, limiting debate to forty minutes and requiring a two-thirds vote of approval, passed the measure. A handful of men (House Ways and Means Committee) wrote the bill in secret, denied citizens the right to express their views, demonstrating disrespect and distrust of their House colleagues, and under such gag procedure denied adequate debate or floor amendment.

The Senate Finance Committee conducted public hearings on the House Bill from January 25 through March 22, 1956. The committee heard 101 witnesses, and a preponderance of them (including AMA spokesmen and the Eisenhower Administration) opposed disability payments. The Senate on July 17, 1956, voted to include a program of payments to the disabled at age 50. The first roll call vote on such disability payments was 47 to 45, Senator Hayden VOTING FOR and Senator Goldwater VOTING AGAINST inclusion thereof. On the roll call vote to "reconsider" immediately following the frist vote, there were 49 "Yeas" and 43 "Nays," Senator Hayden VOTING FOR and Senator Goldwater VOTING AGAINST the disability amendment.

AMERICAN CANCER SOCIETY

NASHVILLE, TENN. — A "radioactive curtain" destroys cancer crumbs spilled during surgery.

This finding by Dr. Horace Goldie of Meharry Medical College has been reported by the American Cancer Society which supports the research.

While Dr. Goldie's studies were with mice, the results strongly suggest that radioactive substances used prophylactically in humans might prevent some recurrences of cancer following surgery.

Dr. Goldie found that a high percentage of mice whose tumors were removed surgically had recurrences due to the spillage of cancer cells into the operative wound. There were far fewer recurrences, on the other hand, among mice treated with radioactive substances at the time of surgery. The radioactivity killed the spilled cancer cells.

The Meharry scientist has poured radioactive yttrium or phosphorus into the wound at the time of operation. These substances, in fluid or colloidal form, bathe the wound and destroy cancer crumbs left at operation.

The radioactive flood also seeps into the lymphatic vessels used by escaping cancer cells and overtakes and destroys some of the cancer

cells. If the cells have spread to distant parts of the body, however, the radioactivity cannot overtake them.

In these studies several types of tumors were used, including cancers which grow in the form of single cells suspended in body fluids.

The radioactive substances used produce a variety of rays – long, far reaching gamma particles which are effective for several yards and narrow ranged beta radiation which strikes only the nearest cells. He has found that phosphorus can be used in the form of insoluble chromic phosphate in higher doses than gold. Phosphorus produces only beta rays; gold radiation is 95.3 per cent beta and 4.7 per cent gamma.

Yttrium has the advantage of remaining in tissues until its radioactivity – effective for about 10 days – is spent. Moreover, a large part of the yttrium applied around tumors creeps inside the tumors and destroys them.

Dr. Goldie and his associates have been able to completely destroy tumors by inserting a radioactive curtain between the tumors and adjacent healthy tissues. This cut off the supply routes to the tumors and starved them. Surgery was simpler and quicker, however; and in these experiments the most effective treatment of mouse cancer was to remove the tumor surgically and use radioactivity prophylactically.

He now is seeking radioactive materials which will track down and destroy cancer cells regardless of where they are in the body.

The scientist has likened cancer to dandelions. If dandelion growths are discovered early they can be extirpated. If they they are dug up but root tips are left, they will regrow. The cautious gardner covers the plumaged tops with a handkerchief to prevent the escape of a cloud of seeds.

Early detection, radical surgery and radioactive curtains are parallel precautions to be taken in treating cancer, he states.

BLUE SHIELD

In June all Arizona Blue Shield Participating Physicians received a communique from G. Robert Barfoot, M.D., president of Blue Shield. The letter carried the caption "It's In The Mill," and its contents are so important to the medical profession as a whole that we thought it might be sagacious at this time to repeat the letter's full contents:

Will be very brief. Thought you should know these things are coming:

1. Surgery in the doctor's office and minor surgery in the outpatient department of the hospital.

2. Diagnostic radiology and pathology coverage for non-hospitalized cases.

3. Additional charge may be made by Participating Physicians to under income subscriber if he has other coverage for the same services in addition to Blue Shield.

4. Payment of additional fees to assisting surgeons in major surgical procedures.

5. Re-evaluation of present fee schedules.

6. Joint commission to investigate desires of Participating Physicians.

These things cannot be put into operation immediately because actuarial study, committee work, legal review, new administrative procedures, and notification of subscribers are involved. However, we will act as quickly as possible and all of them should be completed this year.

In the interest of economy and good public relations, we will try to start most of these things at one time so that notification to you and Blue Shield subscribers can be handled on a "package" basis.

YOU WILL BE NOTIFIED WHEN ANY CHANGES BECOME EFFECTIVE. IN THE MEANTIME DO NOT MAKE ANY CHANGES IN YOUR REGULAR BLUE SHIELD PROCEDURE OR WE MAY BE SUBJECT TO SUIT FOR BREACH OF CONTRACT.

Send us your suggestions and comments – they will be given every consideration in trying to make improvements in your Plan. Since this letter went out, many of the committees have made definite progress on their assigned projects, and much of the thinking regarding the above six points is crystallizing.

ALL CAN PARTICIPATE

Many doctors have inquired as to whether or not they are eligible to participate in the Blue Shield In-Hospital Medical program and provide medical care for Blue Shield members. Any Arizona Blue Shield Participating Physician (and there are over 800 of them) is eligible to receive payment under the Plan for rendering In-Hospital Medical care to the Blue Shield patient.

Woman's AUXILIARY

NURSE RECRUITMENT PROGRAM

The Nurse Recruitment Program in Pima County for the year 1955-56, was highlighted by the fashion show of student nurse uniforms by the Medical Minors Club (Future Nurses Club) of Amphitheatre High School. This show was presented on December 6th to students and their parents interested in nursing. Invitations were extended to the high schools in Tucson. It was shown again on December 12th at the Nurse Recruitment program for the Auxiliary of the Pima County Medical Society.

The Fashion Show was conceived as a vehicle for conveying information to the public about nursing as a career. The Show was commented by Mrs. Leo Kent and the uniforms were modeled by members of the Amphitheatre group.

Mrs. Kent gave a short history of nursing and uniforms representing historical eras were modeled as a contrast to the crisp, efficient uniforms of today. Student nurse uniforms of 8 Schools of Nursing throughout the United States were shown. The commentator directed an informal discussion by the models on the need for nurses, admission and financial requirements, curriculum, types of education available, health programs and student activities. The uniformed Freshman Choir from St. Mary's Hospital School of Nursing made the meeting most impressive by their rendition of choral selections.

The script for the panel discussion was prepared by the State Nurse Recruitment committee chairman, Mrs. D. N. McLeod, Pima County chairman, Mrs. Arthur Dudley, and the students of the Medical Minor group. Informal discussion with the parents by the committee during a refreshment hour cleared up many questions and served to establish a link with the parents for further consultation.

The Nurse Recruitment committee for Pima County included Mrs. Arthur Dudley, chairman, Mrs. D. N. McLeod, ex-officio, Mrs. Sherwood Burr, Mrs. Francis Bean, and Mrs. Robert Pfundt.

The Open House at St. Mary's Hospital during Nurse Recruitment Week was planned by the joint committee on Careers (Recruitment committees from the Auxiliary and the State Nurses Association) and Sister Helen Frances. "The Life of a Student Nurse" was discussed by students from St. Mary's, each in a different phase of training. Enthusiasm was great and many questions came from the audience of future nurses. The movie "Trek of Seven Sisters" was shown, followed by a tour of St. Mary's Hospital. The approximately 150 girls who attended from Tucson and from cities in the southern part of Arizona felt that they had gained a far better insight into nursing as a career.

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